

=> d his ful

(FILE 'HOME' ENTERED AT 11:15:44 ON 06 APR 2006)

FILE 'REGISTRY' ENTERED AT 11:15:51 ON 06 APR 2006

L1 STR
L2 0 SEA SSS SAM L1
L3 2 SEA SSS FUL L1
D SCA

FILE 'HCAPLUS' ENTERED AT 11:21:34 ON 06 APR 2006

L4 1 SEA ABB=ON PLU=ON L3

FILE 'BEILSTEIN' ENTERED AT 11:22:03 ON 06 APR 2006

L5 0 SEA SSS SAM L1
L6 1 SEA SSS FUL L1
L7 1 SEA ABB=ON PLU=ON L6/COM

FILE 'MARPAT' ENTERED AT 11:25:57 ON 06 APR 2006

L8 1 SEA SSS SAM L1
L9 6 SEA SSS FUL L1
L10 2 SEA ABB=ON PLU=ON L9/COM
L*** DEL 2 S L9/COM
L11 1 SEA ABB=ON PLU=ON L10 NOT L4

FILE 'STNGUIDE' ENTERED AT 11:27:38 ON 06 APR 2006

FILE 'REGISTRY' ENTERED AT 11:37:45 ON 06 APR 2006

L12 STR L1
L*** DEL 1 S L12
L13 STR L12
L14 1 SEA SSS SAM L13
D SCA
L15 0 SEA ABB=ON PLU=ON C66/ES AND F/ELS
L16 68869 SEA ABB=ON PLU=ON C6-C6/ES AND F/ELS
L17 892571 SEA ABB=ON PLU=ON C6-C6/ES
L18 0 SEA SUB=L17 SSS SAM L12
L19 142 SEA SUB=L17 SSS FUL L12

FILE 'HCAPLUS' ENTERED AT 11:44:04 ON 06 APR 2006

L20 468 SEA ABB=ON PLU=ON L19
S L13

FILE 'REGISTRY' ENTERED AT 11:44:30 ON 06 APR 2006

L21 3 SEA SUB=L19 SSS SAM L13

FILE 'HCAPLUS' ENTERED AT 11:44:30 ON 06 APR 2006

L22 2 SEA ABB=ON PLU=ON L21

FILE 'REGISTRY' ENTERED AT 11:44:36 ON 06 APR 2006

L23 3 SEA SUB=L19 SSS SAM L13
L24 142 SEA SUB=L19 SSS FUL L13

FILE 'HCAPLUS' ENTERED AT 11:45:41 ON 06 APR 2006

L25 468 SEA ABB=ON PLU=ON L24

FILE 'STNGUIDE' ENTERED AT 11:45:52 ON 06 APR 2006

FILE 'REGISTRY' ENTERED AT 11:55:25 ON 06 APR 2006

L26 STR
L27 0 SEA SUB=L24 SSS SAM L26
L28 22 SEA SUB=L24 SSS FUL L26

FILE 'HCAPLUS' ENTERED AT 12:12:26 ON 06 APR 2006
L29 466 SEA ABB=ON PLU=ON L28
L30 ANALYZE PLU=ON L25 1-468 RN : 8943 TERMS
D

FILE 'REGISTRY' ENTERED AT 12:13:34 ON 06 APR 2006
L31 1 SEA ABB=ON PLU=ON 116644-53-2
D SCA
L32 141 SEA ABB=ON PLU=ON L24 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:14:05 ON 06 APR 2006
L33 71 SEA ABB=ON PLU=ON L32
L34 50 SEA ABB=ON PLU=ON L28 NOT L31

FILE 'REGISTRY' ENTERED AT 12:14:25 ON 06 APR 2006
L35 21 SEA ABB=ON PLU=ON L28 NOT L31

FILE 'HCAPLUS' ENTERED AT 12:14:32 ON 06 APR 2006
L36 69 SEA ABB=ON PLU=ON L35
L37 ANALYZE PLU=ON L36 1-69 RN : 4177 TERMS
D

FILE 'REGISTRY' ENTERED AT 12:16:04 ON 06 APR 2006
L38 1 SEA ABB=ON PLU=ON 116666-63-8
L39 20 SEA ABB=ON PLU=ON L35 NOT L38

FILE 'HCAPLUS' ENTERED AT 12:16:18 ON 06 APR 2006
L40 13 SEA ABB=ON PLU=ON L39
L41 416 SEA ABB=ON PLU=ON L31
L42 63 SEA ABB=ON PLU=ON L38

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4
DICTIONARY FILE UPDATES: 4 APR 2006 HIGHEST RN 879269-14-4

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TSKA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

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FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN
FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,516,393 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

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* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *

NEW

- * PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.
- * NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.

FILE MARPAT

FILE CONTENT: 1961-PRESENT VOL 144 ISS 14 (20060331/ED)

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MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006035965	16	FEB	2006
DE	102004039876	26	JAN	2006
EP	1621541	01	FEB	2006
JP	2006045074	16	FEB	2006
WO	2006012333	02	FEB	2006
GB	2416167	18	JAN	2006
FR	2874013	10	FEB	2006
RU	2267521	10	JAN	2006
CA	2512063	14	JAN	2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Mar 31, 2006 (20060331/UP).

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 12:30:32 ON 06 APR 2006

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FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15

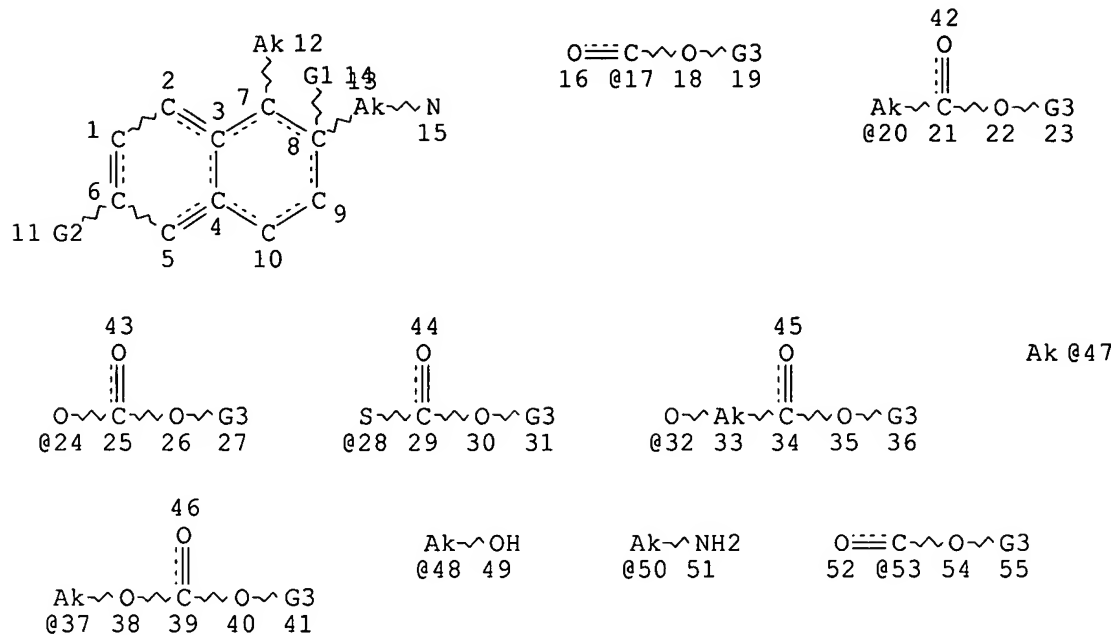
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L1 STR



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VAR G2=X/53

VAR G3=47/48/50

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L3 2 SEA FILE=REGISTRY SSS FUL L1

L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

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L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

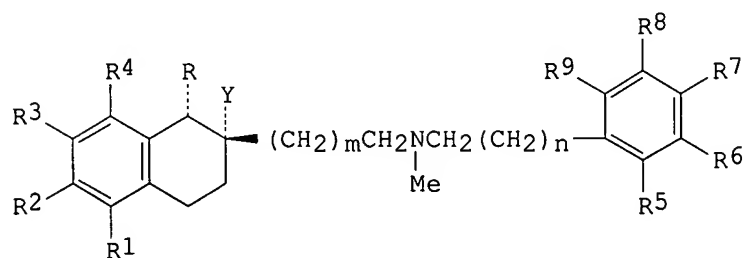
ACCESSION NUMBER: 1987:49807 HCAPLUS

DOCUMENT NUMBER: 106:49807

TITLE: Tetrahydronaphthalene derivatives, their

intermediates, and medicines containing them
 INVENTOR(S): Hengartner, Urs; Ramuz, Henri
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Fed. Rep. Ger.
 SOURCE: Eur. Pat. Appl., 53 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 177960	A2	19860416	EP 1985-112863	19851010
EP 177960	A3	19880113		
EP 177960	B1	19910320		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
FI 8503817	A	19860412	FI 1985-3817	19851002
FI 83508	B	19910415		
FI 83508	C	19910725		
AU 8548301	A1	19860417	AU 1985-48301	19851004
AU 589375	B2	19891012		
ZA 8507681	A	19860528	ZA 1985-7681	19851004
IL 76576	A1	19890131	IL 1985-76576	19851004
JP 61091157	A2	19860509	JP 1985-222893	19851008
HU 38605	A2	19860630	HU 1985-3915	19851009
HU 199773	B	19900328		
CN 85107496	A	19860723	CN 1985-107496	19851009
CN 1007727	B	19900425		
CA 1287636	A1	19910813	CA 1985-492588	19851009
DK 8504648	A	19860412	DK 1985-4648	19851010
NO 8504036	A	19860414	NO 1985-4036	19851010
NO 161971	B	19890710		
NO 161971	C	19891018		
ES 547756	A1	19861116	ES 1985-547756	19851010
US 4680310	A	19870714	US 1985-786253	19851010
AT 61791	E	19910415	AT 1985-112863	19851010
ES 554021	A1	19871216	ES 1986-554021	19860416
ES 554020	A1	19880516	ES 1986-554020	19860416
PRIORITY APPLN. INFO.:			CH 1984-4870	A 19841011
			EP 1985-112863	A 19851010
OTHER SOURCE(S):	MARPAT 106:49807			
GI				



I

AB Tetrahydronaphthalene derivs. I [R = H, alkyl; R1-R4 = H, halo, alkoxy, etc.; R5-R9 = H, halo, Cl-10 alkoxy, alkylthio, ω,ω,ω-trifluoroalkoxy, etc.; Y = OH, alkylcarbonyloxy, alkoxyalkylcarbonyloxy,

alkoxycarbonyloxy, alkoxyalkoxycarbonyloxy, alkylthioalkylcarbonyloxy, (un)substituted benzylcarbonyloxy; m = 1, 2; n = 1, 2, 3] in racemates and optical antipodes, having Ca-antagonistic and antiarrhythmic effects, are prepared. Thus, 2-(p-fluorophenyl)-3-methylbutyric acid was converted to the acid chloride and treated with ethylene in the presence of AlCl_3 to give 6-fluoro-3,4-dihydro-1-isopropyl-2(1H)-naphthalenone, which underwent Grignard reaction with $\text{BrCH}_2\text{CO}_2\text{CMe}_3$, followed by reduction with LiAlH_4 , to give 6-fluoro-1,2,3,4-tetrahydro-2-hydroxy-1 α -isopropyl-2 β -naphthalenylethanol. This intermediate was tosylated, condensed with N-methylhomoveratrylamine, and acylated with methoxyacetyl chloride to give 2-[2-[(3,4-dimethoxyphenylethyl)methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1 α -isopropyl-2 α -naphthyl methoxyacetate-HCl (II). II was tested for Ca-antagonistic and hypotensive effects. A tablet was formulated containing II 75, lactose 135, starch 70, Povidone K 15, talc 3, and Mg stearate 2 mg.

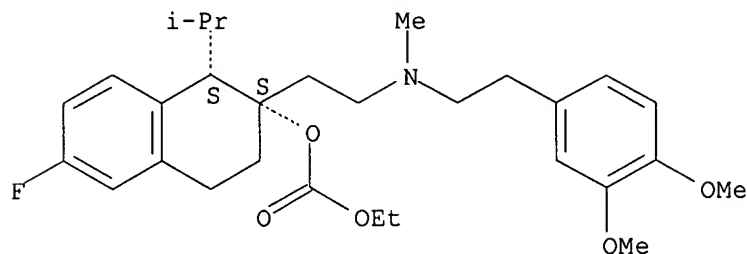
IT 104205-35-8P 104221-42-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as calcium antagonist)

RN 104205-35-8 HCAPLUS

CN Carbonic acid, 2-[2-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ethyl ester, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

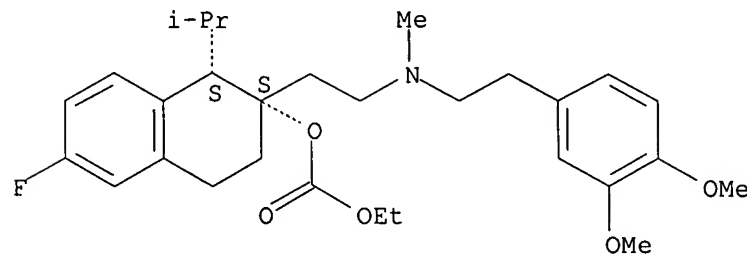


● HCl

RN 104221-42-3 HCAPLUS

CN Carbonic acid, 2-[2-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ethyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=> fil beilst

FILE 'BEILSTEIN' ENTERED AT 12:30:50 ON 06 APR 2006

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FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.

*** FILE CONTAINS 9,516,393 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
separate documents and can not be searched together in one query.
Reaction data for BEILSTEIN compounds may be displayed
immediately with the display codes PRE (preparations) and REA
(reactions). A substance answer set retrieved after the search
for a chemical name, a compounds with available reaction
information by combining with PRE/FA, REA/FA or more generally
with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
between a BEILSTEIN compound and belonging reactions. For mo
detailed reaction searches BRNs can be searched as reaction
partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

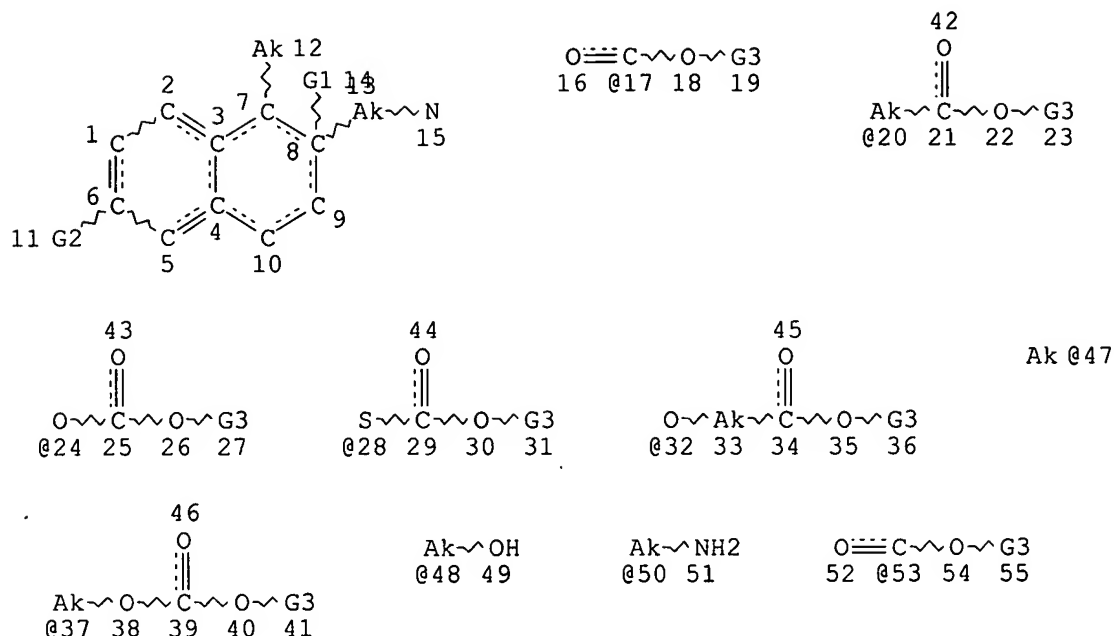
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
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NEW

* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE
SEARCHED, SELECTED AND TRANSFERRED.
* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES,
ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A
COMPOUND AT A GLANCE.

=> d que stat 17

L1 STR



VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L6 1 SEA FILE=BEILSTEIN SSS FUL L1

L7 1 SEA FILE=BEILSTEIN, ABB=ON PLU=ON L6/COM

=> d 17 ide allref

L7 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 8180430

Chemical Name (CN): RO-40-5967

Autonom Name (AUN): carbonic acid 2-(2-<<3-(1H-benzoimidazol-2-

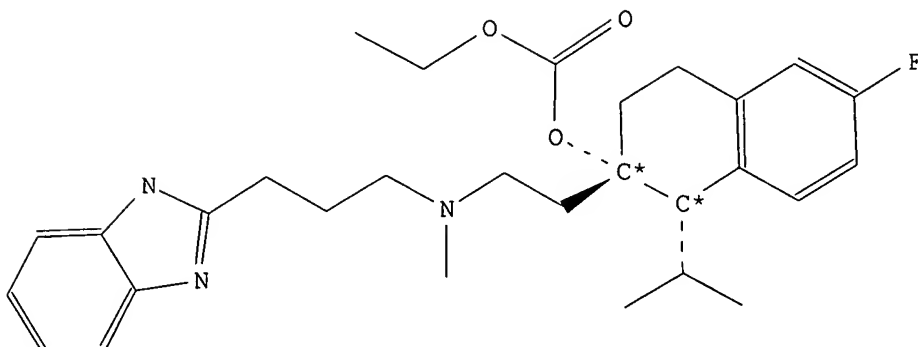
yl)-propyl>-methyl-amino>-ethyl)-6-fluoro-
 1-isopropyl-1,2,3,4-tetrahydro-naphthalen-
 2-yl ester ethyl ester; compound with
 GENERIC INORGANIC NEUTRAL COMPONENT

Fragm. Molec. Formula (FMF): C29 H38 F N3 O3 , Cl H
 Molecular Formula (MF): C29 H38 F N3 O3 . 2 Cl H
 Molecular Weight (MW): 495.64, 36.46
 Fragment BRN (FBRN): 8173779, 1098214
 Lawson Number (LN): 29577, 15006, 2817, 1762, 298
 File Segment (FS): Stereo compound
 Compound Type (CTYPE): heterocyclic
 Constitution ID (CONSID): 6958260
 Tautomer ID (TAUTID): 7721684
 Entry Date (DED): 2000/02/26
 Update Date (DUPD): 2000/02/26

CM 1

FBRN 8173779

FMF C29 H38 F N3 O3



CM 2

FBRN 1098214

FMF Cl H

Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
FMF	Fragment Molecular Formula	2
MF	Molecular Formula	1
FW	Formular Weight	2
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1

TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1
PHARM	Pharmacological Data	1

All References:

ALLREF

1. Rutledge, Aleta; Triggle, David J., Eur.J.Pharmacol., CODEN: EJPHAZ, 280(2), <1995>, 155 - 158; BABS-6131105

=> fil marpat

FILE 'MARPAT' ENTERED AT 12:31:16 ON 06 APR 2006
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FILE CONTENT: 1961-PRESENT VOL 144 ISS 14 (20060331/ED)

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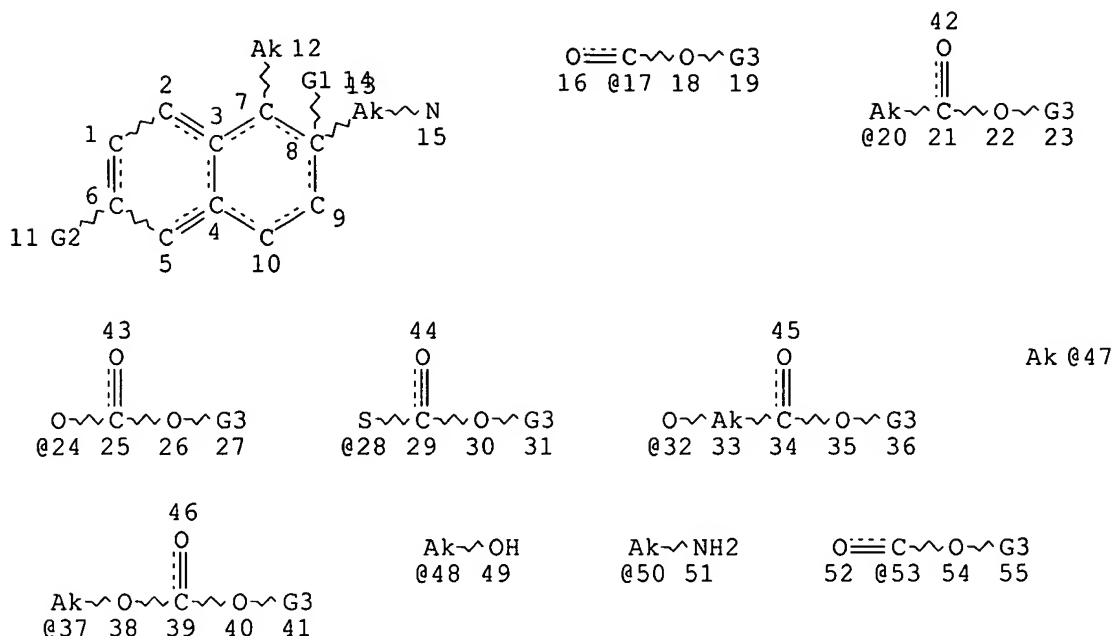
US	2006035965	16	FEB	2006
DE	102004039876	26	JAN	2006
EP	1621541	01	FEB	2006
JP	2006045074	16	FEB	2006
WO	2006012333	02	FEB	2006
GB	2416167	18	JAN	2006
FR	2874013	10	FEB	2006
RU	2267521	10	JAN	2006
CA	2512063	14	JAN	2006

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=> d que stat l11

L1 STR



VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L3 2 SEA FILE=REGISTRY SSS FUL L1

L4 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

L9 6 SEA FILE=MARPAT SSS FUL L1

L10 2 SEA FILE=MARPAT ABB=ON PLU=ON L9/COM

L11 1 SEA FILE=MARPAT ABB=ON PLU=ON L10 NOT L4

=> d l11 ibib abs qhit

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 138:297661 MARPAT

TITLE: Mibefradil-based compounds as calcium channel blockers

INVENTOR(S): useful in the treatment of hypertension and angina
 Druzgala, Pascal; Milner, Peter G.; Pfister, Jurg R.;
 Zhang, Xiaoming
 PATENT ASSIGNEE(S): Aryx Therapeutics, USA
 SOURCE: PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

=> l11 qhit

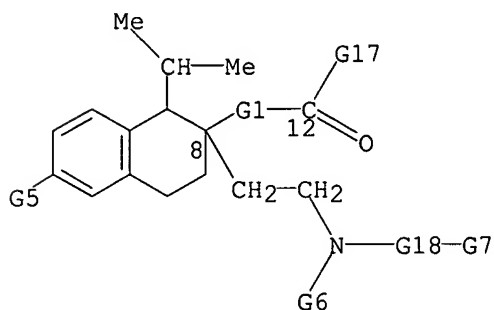
L11 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
 For a list of commands available to you in the current file, enter
 "HELP COMMANDS" at an arrow prompt (=>).

=> d l11 qhit

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN

MSTR 1



G1 = bond
 G3 = Me
 G5 = F
 G17 = 70

70—G3

Patent location: claim 2
 Note: substitution is restricted

=> d l11 ibib abs qhit

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 138:297661 MARPAT

TITLE: Mibefradil-based compounds as calcium channel blockers
 useful in the treatment of hypertension and angina

INVENTOR(S): Druzgala, Pascal; Milner, Peter G.; Pfister, Jurg R.;
 Zhang, Xiaoming

PATENT ASSIGNEE(S): Aryx Therapeutics, USA

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

=> fil hcap
FILE 'HCAPLUS' ENTERED AT 12:32:37 ON 06 APR 2006
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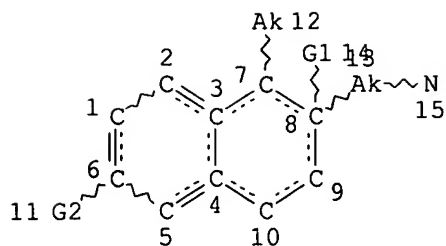
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FILE COVERS 1907 - 6 Apr 2006 VOL 144 ISS 15
FILE LAST UPDATED: 4 Apr 2006 (20060404/ED)

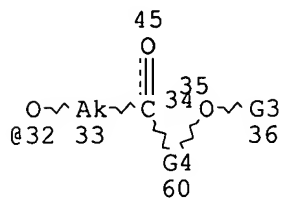
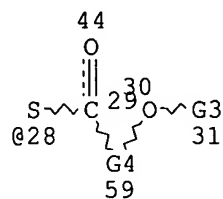
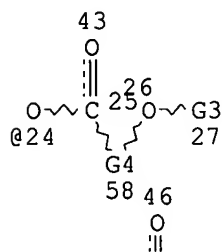
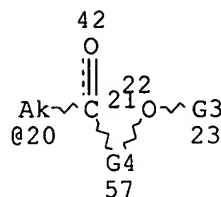
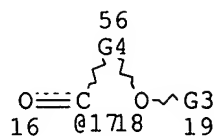
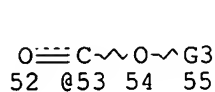
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

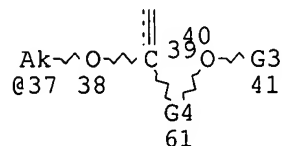
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L12 STR



Ak @47

Ak~OH
@48 49Ak~NH2
@50 51

Page 1-A



Page 2-A

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VAR G2=X/53

VAR G3=47/48/50

REP G4=(0-3) CH2

NODE ATTRIBUTES:

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CONNECT IS E3 RC AT 15

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CONNECT IS E2 RC AT 37

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GGCAT IS LIN SAT AT 20

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GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

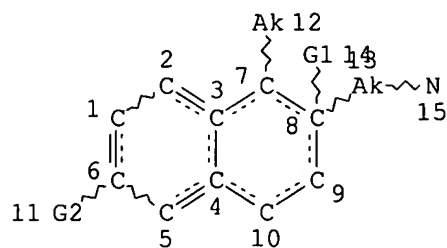
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

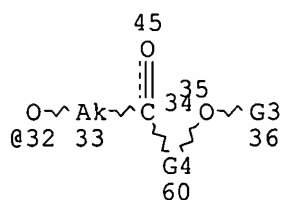
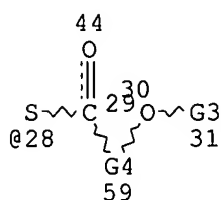
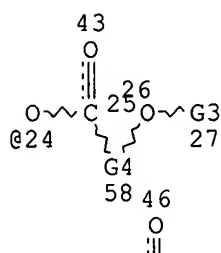
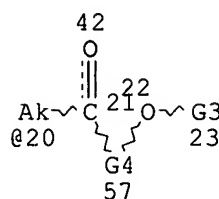
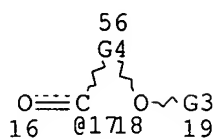
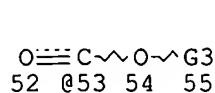
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STEREO ATTRIBUTES: NONE

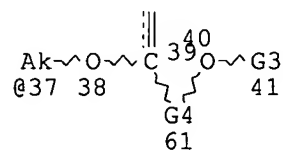
L13 STR



Ak @47

Ak~OH
@48 49Ak~NH2
@50 51

Page 1-A



Page 2-A

VAR G1=17/20/24/28/32/37

VAR G2=X/53

VAR G3=47/48/50

REP G4=(0-1) CH2

NODE ATTRIBUTES:

CONNECT IS E3 RC AT 7

CONNECT IS E1 RC AT 12

CONNECT IS E3 RC AT 15

CONNECT IS E2 RC AT 20

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E1 RC AT 47

DEFAULT MLEVEL IS ATOM

GGCAT IS LOC AT 12

GGCAT IS LIN SAT AT 20

GGCAT IS LIN SAT AT 33

GGCAT IS LIN SAT AT 37

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 61

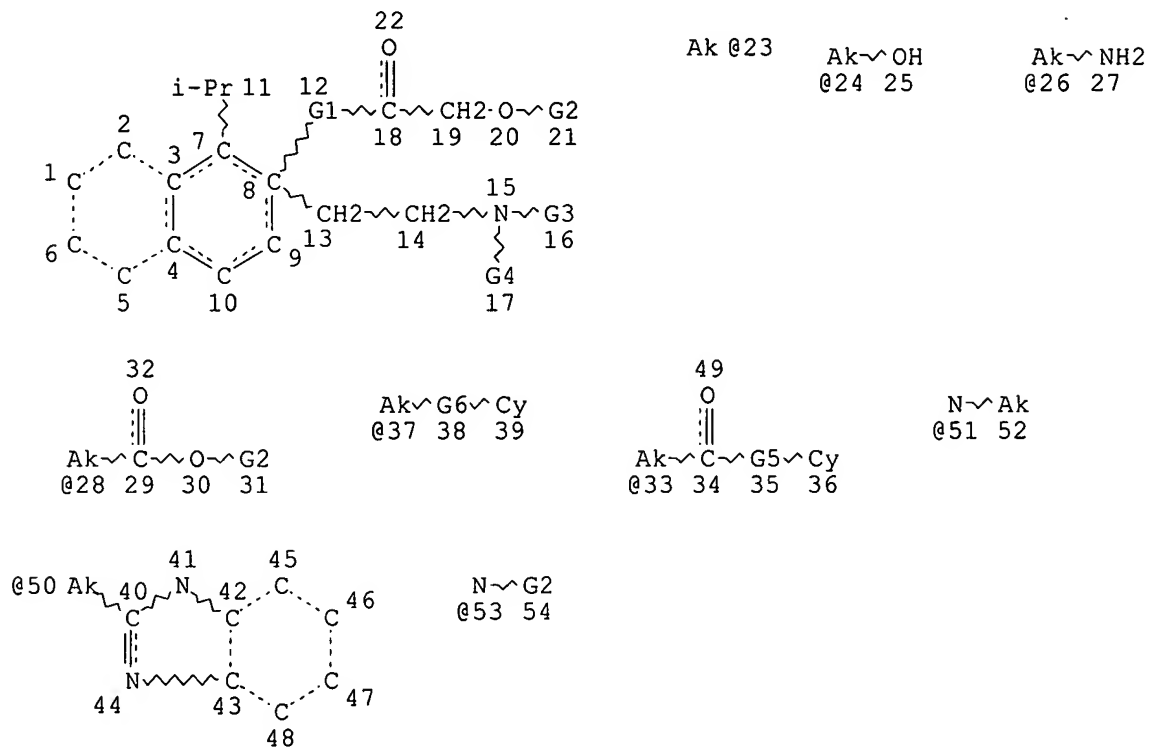
STEREO ATTRIBUTES: NONE

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L24 142 SEA FILE=REGISTRY SUB=L19 SSS FUL L13

L26 STR



REP G1=(0-6) A

VAR G2=23/24/26

VAR G3=ME/28

VAR G4=33/37/50

VAR G5=O/NH/51

VAR G6=O/S/NH/53

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 23

CONNECT IS E2 RC AT 28

CONNECT IS E2 RC AT 33

CONNECT IS E2 RC AT 37

CONNECT IS E2 RC AT 41

CONNECT IS E2 RC AT 50

CONNECT IS E1 RC AT 52

DEFAULT MLEVEL IS ATOM

GGCAT IS LIN LOC SAT AT 28

GGCAT IS LIN LOC SAT AT 33

GGCAT IS LIN LOC SAT AT 37

GGCAT IS LIN LOC SAT AT 50

GGCAT IS LOC AT 52

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE

L28 22 SEA FILE=REGISTRY SUB=L24 SSS FUL L26
L31 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116644-53-2
L35 21 SEA FILE=REGISTRY ABB=ON PLU=ON L28 NOT L31
L38 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116666-63-8
L39 20 SEA FILE=REGISTRY ABB=ON PLU=ON L35 NOT L38
L40 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L39

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L40 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:531365 HCAPLUS

DOCUMENT NUMBER: 141:65063

TITLE: Use of a combination containing a non-nucleoside
reverse transcriptase inhibitor (NNRTI) with an
inhibitor of cytochrome p450 for the treatment of
HIV-1 infection

INVENTOR(S): Cordingley, Michael Graham

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054586	A1	20040701	WO 2003-EP14224	20031215
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2510143	AA	20040701	CA 2003-2510143	20031215
AU 2003296647	A1	20040709	AU 2003-296647	20031215
US 2004152625	A1	20040805	US 2003-736301	20031215
EP 1575595	A1	20050921	EP 2003-813119	20031215
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003017095	A	20051025	BR 2003-17095	20031215
NO 2005003455	A	20050810	NO 2005-3455	20050715
PRIORITY APPLN. INFO.:			US 2002-433690P	P 20021216
			WO 2003-EP14224	W 20031215

AB An improved method for using a NNRTI in the treatment of HIV-1 infection comprises administering to a human in need of treatment for HIV-1 infection a therapeutically effective amount of the NNRTI, or a

pharmaceutically acceptable salt thereof, and an amount of an inhibitor of cytochrome P 450 that is sufficient to elevate, enhance, or extend plasma concns. of said NNRTI.

IT 710282-37-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

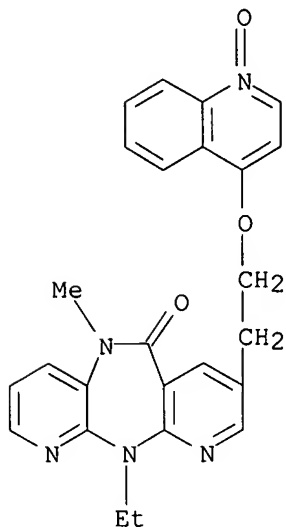
RN 710282-37-4 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, mixt. with 11-ethyl-5,11-dihydro-5-methyl-8-[2-[(1-oxido-4-quinolinyl)oxy]ethyl]-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one (9CI) (CA INDEX NAME)

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CRN 380378-81-4

CMF C25 H23 N5 O3

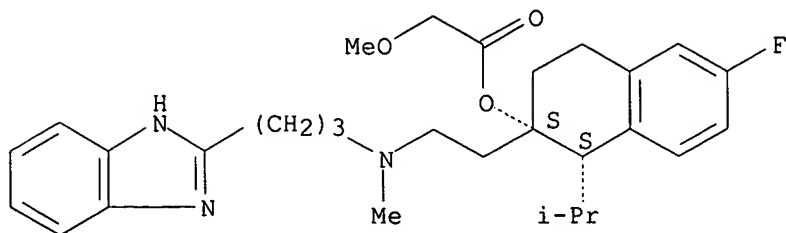


CM 2

CRN 116644-53-2

CMF C29 H38 F N3 O3

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:405028 HCAPLUS

DOCUMENT NUMBER: 133:217516

TITLE: High affinity interaction of mibefradil with voltage-gated calcium and sodium channels

AUTHOR(S): Eller, Philipp; Berjukov, Stanislav; Wanner, Siegmund; Huber, Irene; Hering, Steffen; Knaus, Hans-Gunther; Toth, Geza; Kimball, S. David; Striessnig, Jorg

CORPORATE SOURCE: Institut fur Biochemische Pharmakologie, Innsbruck, A-6020, Austria

SOURCE: British Journal of Pharmacology (2000), 130(3), 669-677

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mibefradil is a novel Ca²⁺ antagonist which blocks both high-voltage activated and low voltage-activated Ca²⁺ channels. Although L-type Ca²⁺ channel block was demonstrated in functional expts. its mol. interaction with the channel has not yet been studied. We therefore investigated the binding of [3H]-mibefradil and a series of mibefradil analogs to L-type Ca²⁺ channels in different tissues. [3H]-Mibefradil labeled a single class of high affinity sites on skeletal muscle L-type Ca²⁺ channels (KD of 2.5±0.4 nM, Bmax = 56.4±2.3 pmol mg⁻¹ of protein). Mibefradil (and a series of analogs) partially inhibited (+)-[3H]-isradipine binding to skeletal muscle membranes but stimulated binding to brain L-type Ca²⁺ channels and α₁C-subunits expressed in tsA201 cells indicating a tissue-specific, non-competitive interaction between the dihydropyridine and mibefradil binding domain. [3H]-Mibefradil also labeled a heterogeneous population of high affinity sites in rabbit brain which was inhibited by a series of nonspecific Ca²⁺ and Na⁺-channel blockers. Mibefradil and its analog R040-6040 had high affinity for neuronal voltage-gated Na⁺-channels as confirmed in binding (apparent K_i values of 17 and 1.0 nM, resp.) and functional expts. (40% use-dependent inhibition of Na⁺-channel current by 1 μM mibefradil in GH3 cells). Our data demonstrate that mibefradil binds to voltage-gated L-type Ca²⁺ channels with very high affinity and is also a potent blocker of voltage-gated neuronal Na⁺-channels. More lipophilic mibefradil analogs may possess neuroprotective properties like other nonselective Ca²⁺-/Na⁺-channel blockers.

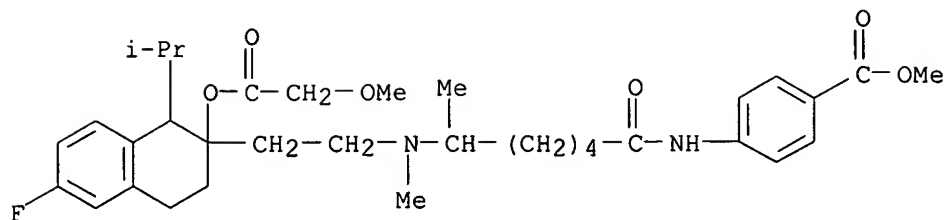
IT 291307-58-9, Ro 19-8287

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high affinity interaction of mibeadil with voltage-gated calcium and sodium channels)

RN 291307-58-9 HCAPLUS

CN Benzoic acid, 4-[[[6-[[2-[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxyacetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]-1-oxoheptyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



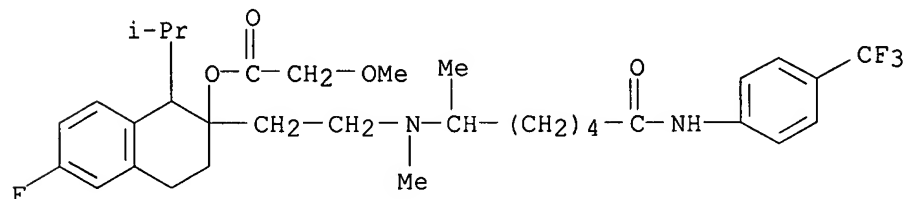
IT 291307-57-8, Ro 19-6945

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high affinity interaction of mibefradil with voltage-gated calcium and sodium channels)

RN 291307-57-8 HCAPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-[2-[methyl[1-methyl-6-oxo-6-[[4-(trifluoromethyl)phenyl]amino]hexyl]amino]ethyl]-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:819361 HCAPLUS

DOCUMENT NUMBER: 132:44979

TITLE: Nitrate salts of antihypertensive medicines

INVENTOR(S): Del, Soldato Piero

PATENT ASSIGNEE(S): Nicox S. A., Fr.

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967231	A1	19991229	WO 1999-EP4138	19990615
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, IL, IN, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
IT 1301759	B1	20000707	IT 1998-MI1408	19980619
CA 2335356	AA	19991229	CA 1999-2335356	19990615

AU 9945139	A1	20000110	AU 1999-45139	19990615
AU 770387	B2	20040219		
EP 1087953	A1	20010404	EP 1999-927990	19990615
EP 1087953	B1	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO

BR 9911305	A	20011023	BR 1999-11305	19990615
JP 2002518492	T2	20020625	JP 2000-555885	19990615
RU 2235097	C2	20040827	RU 2000-131690	19990615
AT 282600	E	20041215	AT 1999-927990	19990615
ES 2234265	T3	20050616	ES 1999-927990	19990615
ZA 2000006136	A	20020130	ZA 2000-6136	20001030
US 6645965	B1	20031111	US 2000-719164	20001212
US 2004147575	A1	20040729	US 2003-671746	20030929

PRIORITY APPLN. INFO.:

IT 1998-MI1408	A	19980619
WO 1999-EP4138	W	19990615
US 2000-719164	A3	20001212

OTHER SOURCE(S): MARPAT 132:44979

AB Nitric acid salts of drugs have antihypertensive activity. Some example salts prepared and showing antihypertensive activity were: timolol, propranolol, sildenafil, valsartan, hydralazine, nicardipine, verapamil, and amiloride nitrate salts.

IT 252951-80-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrate salts of antihypertensive medicines)

RN 252951-80-7 HCAPLUS

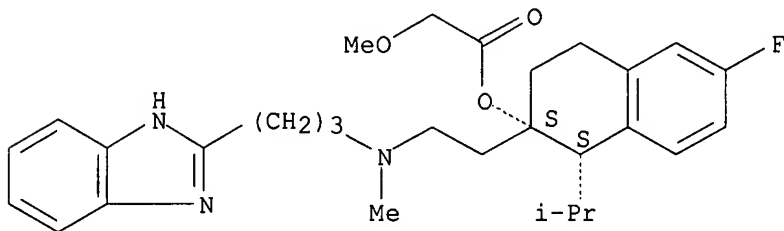
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, nitrate (9CI) (CA INDEX NAME)

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CRN 116644-53-2

CMF C29 H38 F N3 O3

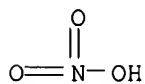
Absolute stereochemistry.



CM 2

CRN 7697-37-2

CMF H N O3



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:104627 HCAPLUS
DOCUMENT NUMBER: 130:205140
TITLE: Potential-dependent, T-type calcium channel inhibitors for treatment or prevention of pollakiuria or urinary incontinence
INVENTOR(S): Narita, Kazuhisa; Koga, Ichiro; Okada, Atsushi
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11035483	A2	19990209	JP 1998-128463	19980512

PRIORITY APPLN. INFO.: JP 1997-144503 A 19970520

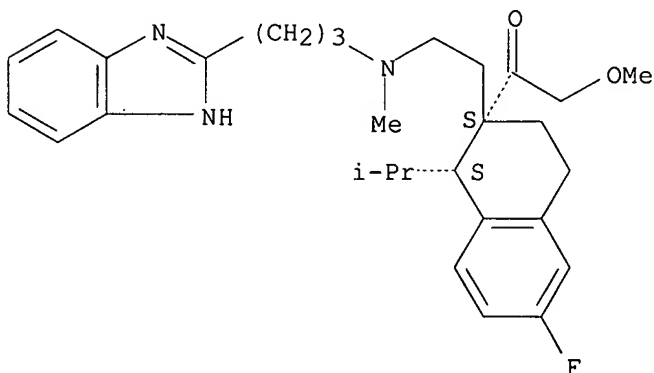
AB Potential-dependent, T-type calcium channel inhibitors e.g. [1S, 2S]-2-[2-[[3-[2-benzimidazolyl]propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthylmethoxyacetate and 7-[4-[4,4'-difluorobenzohydril]piperadino-1-methyl]-2-[[2-hydroxyethyl]amino]-4-isopropyl-2,4,6-cycloheptatrien-1-one for treatment or prevention of pollakiuria or urinary incontinence are claimed.

IT 220873-01-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potential-dependent, T-type calcium channel inhibitors for treatment or prevention of pollakiuria or urinary incontinence)

RN 220873-01-8 HCAPLUS

CN Ethanone, 1-[(1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:721683 HCAPLUS

DOCUMENT NUMBER: 129:330729
 TITLE: Preparation of mibefradil I.
 INVENTOR(S): Fleming, Michael Paul; Harrington, Peter John
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849149	A1	19981105	WO 1998-EP2416	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876477	A1	19981124	AU 1998-76477	19980423
PRIORITY APPLN. INFO.:			US 1997-45151P	P 19970430
			WO 1998-EP2416	W 19980423

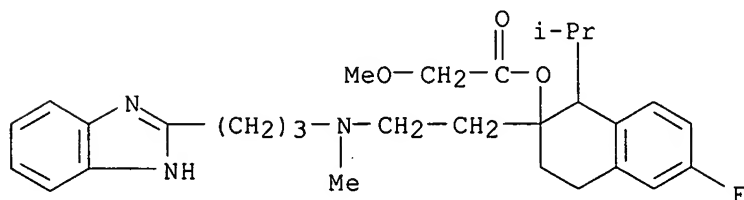
OTHER SOURCE(S): CASREACT 129:330729

AB 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate was prepared by reducing N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide to give 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol and contacting the latter with MeOCH₂CO₂H or an activated derivative thereof.

IT 213272-70-9P, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate 213272-71-0P, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate dihydrochloride
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of mibefradil)

RN 213272-70-9 HCAPLUS

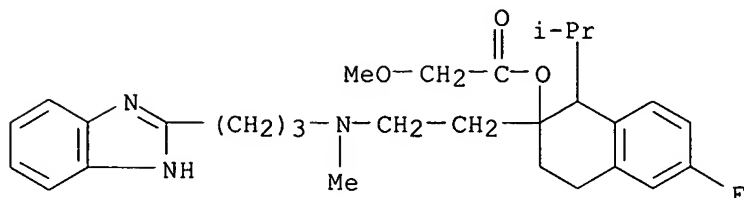
CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



RN 213272-71-0 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:721682 HCAPLUS
 DOCUMENT NUMBER: 129:343493
 TITLE: Preparation of mibefradil II.
 INVENTOR(S): Harrington, Peter John; Wong, Jim-wah
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849148	A1	19981105	WO 1998-EP2415	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9879092	A1	19981124	AU 1998-79092	19980423
PRIORITY APPLN. INFO.:			US 1997-46795P	P 19970430
			WO 1998-EP2415	W 19980423

OTHER SOURCE(S): CASREACT 129:343493

AB A process for preparation of 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate via contacting (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid or an activated derivative thereof with [3-(1H-benzimidazol-2-yl)propyl]methylamine to form N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide is claimed.

IT **213272-70-9P**, 2-[2-[[3-(1H-Benzimidazol-2-yl) propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate

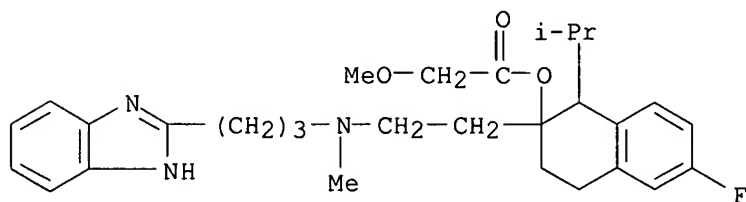
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

(preparation of mibefradil)

RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:721681 HCAPLUS

DOCUMENT NUMBER: 129:343492

TITLE: Preparation of mibefradil III.

INVENTOR(S): Harrington, Peter John; Wong, Jim-wah

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849147	A1	19981105	WO 1998-EP2406	19980423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876473	A1	19981124	AU 1998-76473	19980423
PRIORITY APPLN. INFO.:			US 1997-45150P	P 19970430
			WO 1998-EP2406	W 19980423

OTHER SOURCE(S): CASREACT 129:343492

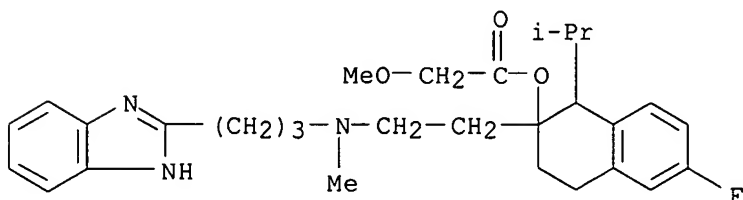
AB 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate was prepared by contacting [3-(1H-benzimidazol-2-yl)propyl]methylamine with (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile in the presence of H₂ and a hydrogenation catalyst, followed by contacting the resulting 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol with MeOCH₂CO₂H or an activated derivative thereof.

IT 213272-70-9P, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
(Preparation)
(preparation of mibefradil)

RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:618399 HCAPLUS

DOCUMENT NUMBER: 129:245150

TITLE: Improved preparation of mibefradil via an acetonitrile anion

INVENTOR(S): Wong, Jim-wah; Harrington, Peter J.

PATENT ASSIGNEE(S): Roche Colorado Corp., USA

SOURCE: U.S., 6 pp.

CODEN: USXXAM

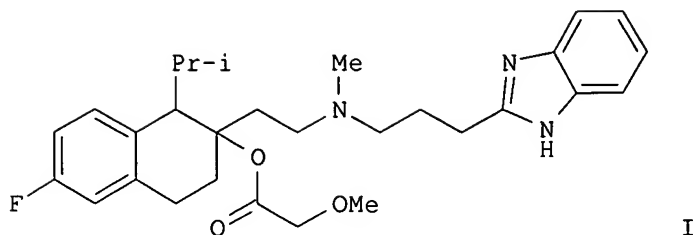
DOCUMENT TYPE: Patent

LANGUAGE: English

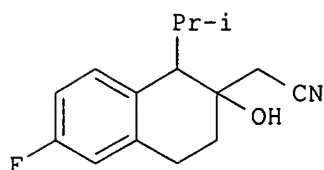
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

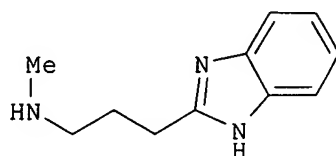
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811557	A	19980922	US 1998-60401	19980414
PRIORITY APPLN. INFO.:			US 1998-60401	19980414
OTHER SOURCE(S):		CASREACT 129:245150		
GI				



I

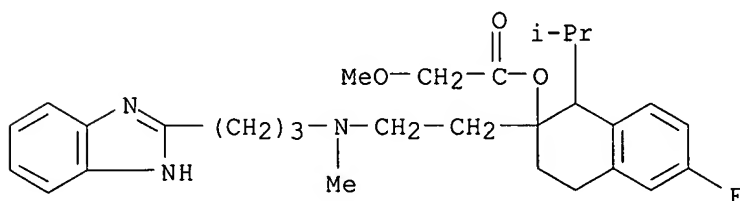


II



III

- AB A method of preparing 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate (I) comprises contacting 6-fluoro-1-isopropyl-3,4-dihydro-1H-naphthalen-2-one with the anion of acetonitrile in an aprotic polar solvent, contacting the thus-formed (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile (II) with [3-(1H-benzimidazol-2-yl)propyl]methylamine (III) in the presence of hydrogen and a hydrogenation catalyst, and finally esterifying the obtained 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-ol with methoxyacetic acid or an activated derivative of it. The invention is particularly applicable to the preparation of the antihypertensive mibefradil, namely (1S,2S)-I, and its di-HCl salt. The intermediate nitrile II is a new compound
- IT **213272-70-9P**, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (improved preparation of mibefradil via an acetonitrile anion)
- RN 213272-70-9 HCAPLUS
- CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

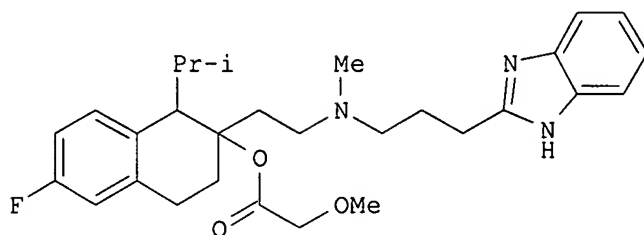


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

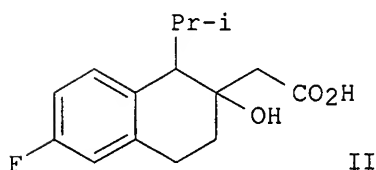
L40 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:618398 HCAPLUS
 DOCUMENT NUMBER: 129:245149
 TITLE: Improved preparation of mibefradil via a naphthalenylacetic acid
 INVENTOR(S): Harrington, Peter J.; Wong, Jim-wah
 PATENT ASSIGNEE(S): Roche Colorado Corp., USA
 SOURCE: U.S., 7 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

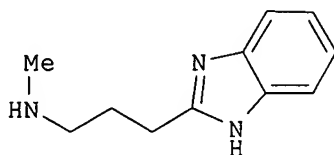
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811556	A	19980922	US 1998-60168	19980414
PRIORITY APPLN. INFO.:			US 1998-60168	19980414
OTHER SOURCE(S):	CASREACT 129:245149			
GI				



I



II



III

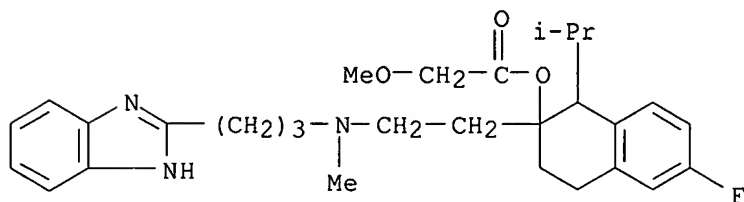
AB A method of preparing 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate (I) comprises contacting (6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid (II) or an activated derivative with [3-(1H-benzimidazol-2-yl)propyl]methylamine (III), reducing the formed amide function to a tertiary amine, and esterifying the obtained hydroxy amine with methoxyacetic acid or an activated derivative of it. The invention is particularly applicable to the preparation of the antihypertensive mibefradil, i.e., (1S,2S)-I, and its di-HCl salt. The intermediate amide, namely N-[3-(1H-benzimidazol-2-yl)propyl]-2-(6-fluoro-2-hydroxy-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl)-N-methylacetamide, is a new compound
 IT **213272-70-9P**, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate **213272-71-0P**, 2-[2-[[3-(1H-Benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1-isopropyl-1,2,3,4-tetrahydronaphthalen-2-yl methoxyacetate dihydrochloride
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

(preparation of mibefradil via a naphthalenylacetic acid)

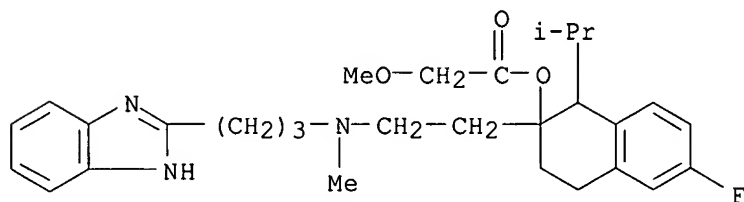
RN 213272-70-9 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)



RN 213272-71-0 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:424055 HCAPLUS

DOCUMENT NUMBER: 127:144696

TITLE: Metabolism of the calcium antagonist, mibefradil (POSICOR, Ro 40-5967). Part III. Comparative pharmacokinetics of mibefradil and its major metabolites in rat, marmoset, cynomolgus monkey and man

AUTHOR(S): Wiltshire, H. R.; Sutton, B. M.; Heeps, G.; Betty, A. M.; Angus, D. W.; Harris, S. R.; Worth, E.; Welker, H. A.

CORPORATE SOURCE: Department of Pharmacokinetics and Metabolism, Roche Products Ltd, Welwyn Garden City, AL7 3AY, UK

SOURCE: Xenobiotica (1997), 27(6), 557-571
CODEN: XENOBH; ISSN: 0049-8254

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1. The metabolism of mibefradil has been examined in rat, marmoset, cynomolgus monkey and man after single and multiple oral administration. 2.

Metabolites typically represent between 50 and 80% of the circulating drug-related material after single oral doses of mibefradil to man, rat and marmoset. They arise by a combination of enzymic processes: cytochrome P 450-mediated oxidation at saturated and unsatd. carbon atoms, cytochrome P 450-catalyzed dealkylation and hydrolysis of the ester side-chain. 3. Plasma levels of mibefradil in the cynomolgus monkey are extremely low as a result of very efficient first-pass hydrolysis of its side-chain to give the corresponding alc. Steady-state concns. of this metabolite are comparable with those of the parent drug in man and marmoset, but are relatively low in rat plasma. 4. Hydroxylation at the benzylic carbon of the tetrahydronaphthyl ring leads to further important metabolites in primates, whereas the products of O- and N-demethylation are found in small amts. in all four species. 5. Ests. of the exposure of the various species to the principal metabolites indicate that the choice of the rat, marmoset and cynomolgus monkey for the toxicol. assessment of mibefradil was appropriate.

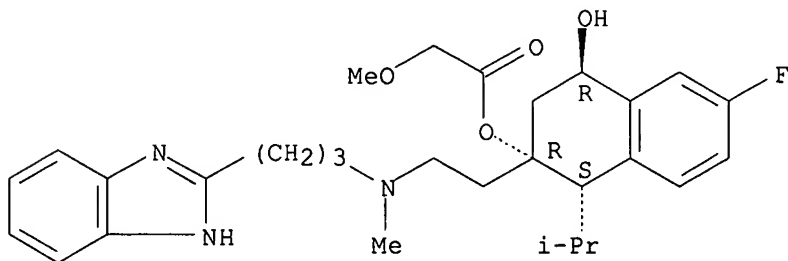
IT 193351-45-0

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(metabolism of the calcium antagonist mibefradil in humans and lab animals)

RN 193351-45-0 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1 α ,2 α ,4 β)]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:424054 HCAPLUS

DOCUMENT NUMBER: 127:144695

TITLE: Metabolism of the calcium antagonist, mibefradil (POSICOR, Ro 40-5967). Part II. Metabolism in hepatic microsomes from rat, marmoset, cynomolgus monkey, rabbit and man

AUTHOR(S): Wiltshire, H. R.; Sutton, B. M.; Heeps, G.; Betty, A. M.; Angus, D. W.; Madigan, M. J.; Sharp, S. R.

CORPORATE SOURCE: Pharmacokinetics and Metabolism Department, Roche Products Ltd, Welwyn Garden City, AL7 3AY, UK

SOURCE: Xenobiotica (1997), 27(6), 539-556
CODEN: XENOBH; ISSN: 0049-8254

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The calcium antagonist, mibefradil, is converted to some 30 metabolites after incubation with hepatic microsomes from the rat, marmoset, cynomolgus monkey, rabbit and man. The wide inter-species differences in

metabolic profile stem mainly from variations in the activity of the microsomal esterase, which hydrolyses the ester side-chain of mibefradil to give the alc. metabolite, Ro 40-5966. Hydrolysis is especially marked in the

cynomolgus monkey and rabbit, less in man and least in the rat and marmoset. The biotransformation of this alc. metabolite by cytochromes P 450 is more facile than that of the parent compound, leads to fewer metabolites and the metabolic profiles in all species are similar. The most important cytochrome P 450-mediated metabolic process in microsomes in all species is hydroxylation at the benzylic carbon atom of the tetrahydronaphthyl group; further oxidation of the resultant secondary alc. to a ketone also occurs. These reactions indicate the route of the biosynthetic pathway which leads to the major, naphthyl-glucuronide metabolites previously isolated from rat bile. Dealkylation of the tertiary amino group is also important and leads to compds. lacking either the N-Me group or the propylbenzimidazole moiety. Hydroxylation of the benzimidazole ring at both the 4- and 5-positions is largely restricted to mibefradil and does not occur to a significant extent with Ro 40-5966.

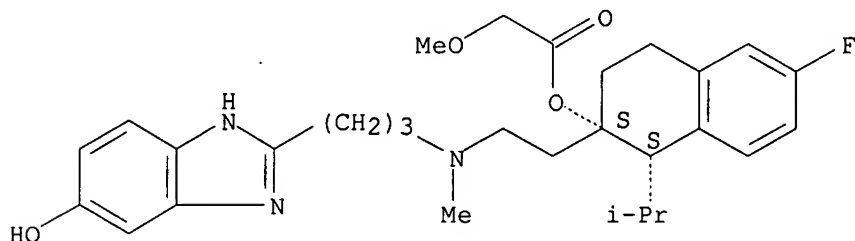
IT 144917-60-2 193351-45-0 193464-93-6
193464-95-8

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(metabolism of the calcium antagonist mibefradil in humans and lab animals)

RN 144917-60-2 HCAPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(5-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

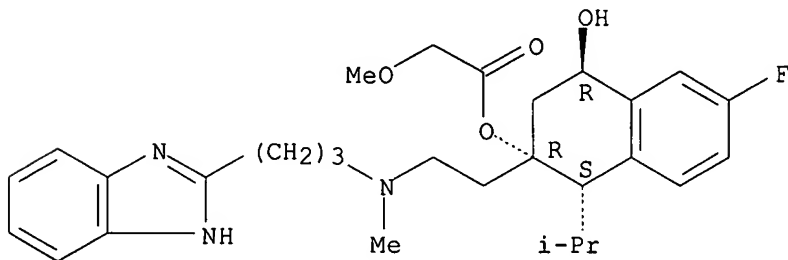
Absolute stereochemistry.



RN 193351-45-0 HCAPLUS

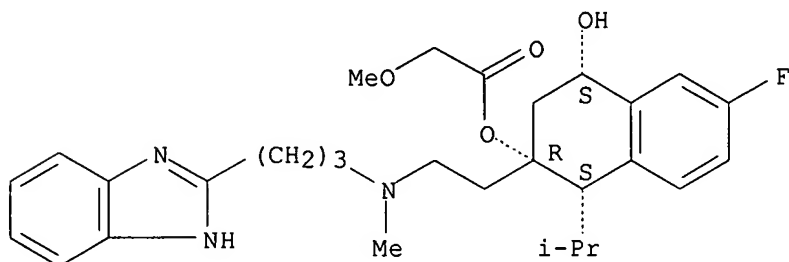
CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1 α ,2 α ,4 β)]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



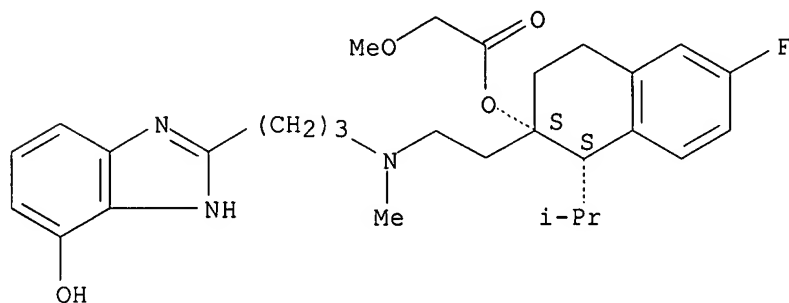
RN 193464-93-6 HCAPLUS
 CN Acetic acid, methoxy-, 2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-4-hydroxy-1-(1-methylethyl)-2-naphthalenyl ester, [1S-(1 α ,2 α ,4 α)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 193464-95-8 HCAPLUS
 CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(4-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:15784 HCAPLUS

DOCUMENT NUMBER: 118:15784

TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway

AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.; Kozlowski, U. M.; Worth, E.

CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK

SOURCE: Xenobiotica (1992), 22(7), 837-57
 CODEN: XENOBH; ISSN: 0049-8254

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The calcium antagonist, Ro 40-5967, is metabolized to a multitude of products by the rat and drug-related material is excreted predominantly via the bile. Diode-array, UV spectroscopy, following reverse phase HPLC separation of the partially purified metabolites, has been used to classify

these compds. into six spectral classes which have been correlated with different metabolic reactions. Connection of a mass spectrometer directly to the HPLC equipment by a thermospray interface, produced useful mass spectra. These, together with the UV spectra, enabled the structures of many metabolites to be elucidated. Confirmation of structural assignments was provided by NMR spectra of the major metabolites. Major metabolite pathways included N-demethylation (16% of the biliary metabolites), hydrolysis of the ester side-chain (32%), hydroxylation at 4- (19%) and 5- (29%) positions of the benzimidazole ring, aromatization of the tetrahydronaphthyl system (26%), loss of the benzimidazole (15%) and glucuronidation of hydroxyl groups (81%).

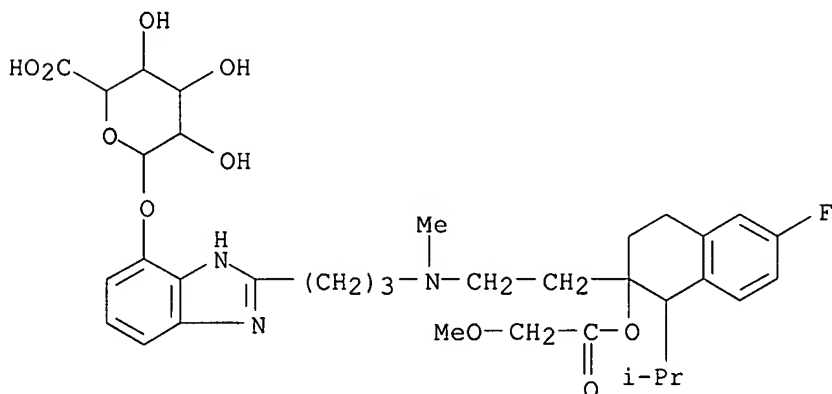
IT 144917-55-5 144917-60-2 144917-61-3
144917-69-1

RL: PROC (Process)

(as Ro 5967 metabolite, characterization of, by diode-array UV spectroscopy and thermospray-mass spectrometry)

RN 144917-55-5 HCAPLUS

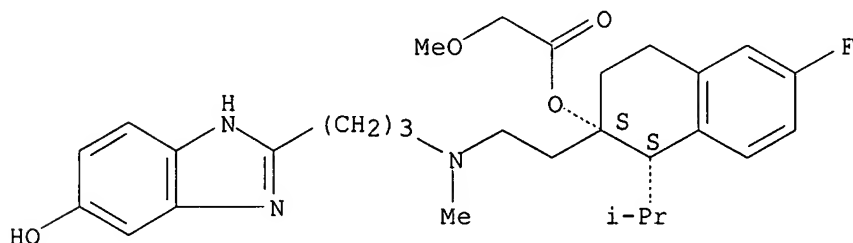
CN β -D-Glucopyranosiduronic acid, 2-[3-[[2-[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxyacetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]propyl]-1H-benzimidazol-4-yl, (1S-cis)- (9CI) (CA INDEX NAME)



RN 144917-60-2 HCAPLUS

CN Acetic acid, methoxy-, 6-fluoro-1,2,3,4-tetrahydro-2-[2-[[3-(5-hydroxy-1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-1-(1-methylethyl)-2-naphthalenyl ester, (1S-cis)- (9CI) (CA INDEX NAME)

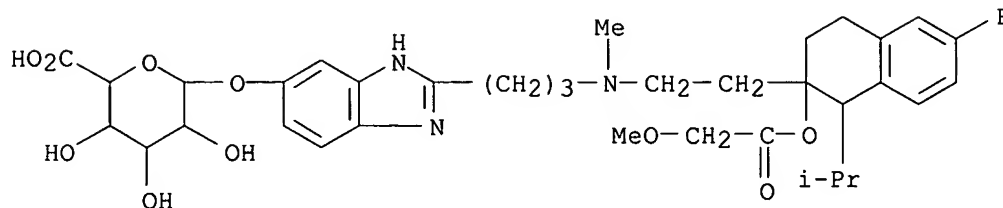
Absolute stereochemistry.



RN 144917-61-3 HCAPLUS

CN β -D-Glucopyranosiduronic acid, 2-[3-[[2-[6-fluoro-1,2,3,4-tetrahydro-2-[(methoxyacetyl)oxy]-1-(1-methylethyl)-2-naphthalenyl]ethyl]methylamino]

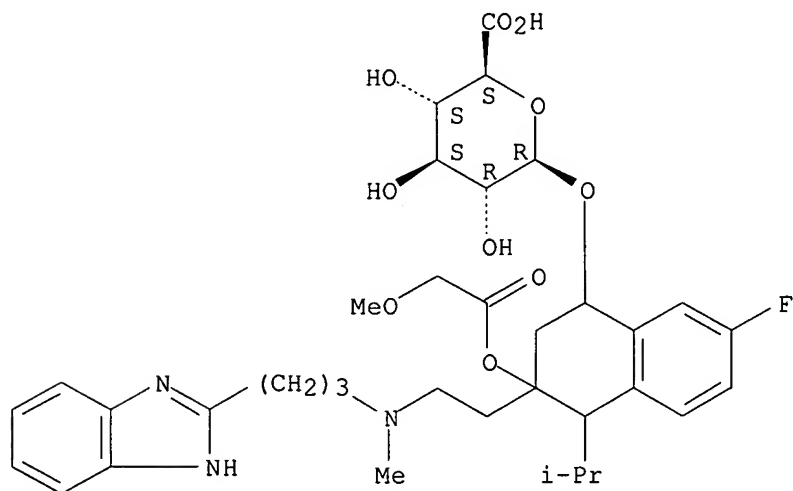
propyl]-1H-benzimidazol-5-yl, (1S-cis)- (9CI) (CA INDEX NAME)



RN 144917-69-1 HCAPLUS

CN β -D-Glucopyranosiduronic acid, 3-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-7-fluoro-1,2,3,4-tetrahydro-3-[(methoxyacetyl)oxy]-4-(1-methylethyl)-1-naphthalenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:549535 HCAPLUS

DOCUMENT NUMBER: 109:149535

TITLE: Preparation of [[(heterocyclylalkyl)amino]ethyl]tetrahydronaphthalenes as cardiovascular agents

INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerki, Hans Peter; Marti, Fraenzi; Ramuz, Henri

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE: Eur. Pat. Appl., 37 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

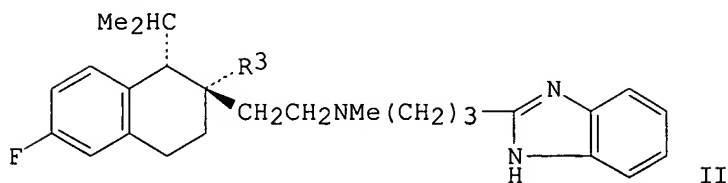
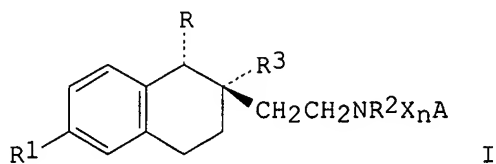
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8705599	A	19880515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		
PRIORITY APPLN. INFO.:			CH 1986-4565	A 19861114
			EP 1987-116251	A 19871104
OTHER SOURCE(S):			MARPAT 109:149535	
GI				



AB The title compds. [I; A = substituted 2-(imidazol-2-yl)ethyl, (un)substituted benzimidazolyl, benzothiazolyl, etc.; R, R2 = alkyl; R1 = halo; R3 = OH, alkoxy, alkanoyloxy, alkoxyalkanoyloxy, etc.; X = C1-18 alkylene, optionally interrupted by 1,4-phenylene or -cyclohexylene; n = 0, 1] were prepared PhCH2O2CNMe(CH2)3CONHC6H4NH2-2 (preparation given) was refluxed 2 h in PhMe containing 4-MeC6H4SO3H and the product hydrogenolized over Pd/C to give 2-[3-(methylamino)propyl]benzimidazole which was heated 30 min at 120° in (Me2CH)2NEt with 2-(6-fluoro-1,2,3,4-tetrahydro-2-hydroxy-1 α -isopropyl-2 β -naphthyl)ethyl p-toluenesulfonate to give title compound II (R3 = OH). The latter was stirred overnight with MeOCH2COCl in CHCl3 containing (Me2CH)2NEt to give II (R3 = MeOCH2CO2) (III)

which, at 0.3 mg/kg i.v., gave 25% and 86% increase in heart contractility and coronary blood flow, resp., in anesthetized dogs. Tablets were prepared each containing III 75, lactose 135, starch 70, Povidone K 30 15, talc 3, and Mg stearate 2 mg.

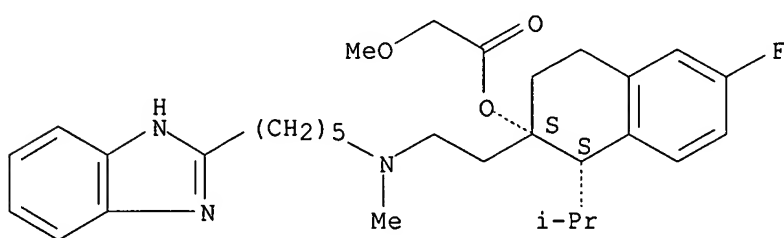
IT 116666-65-0P 116666-76-3P 116666-93-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiovascular agent)

RN 116666-65-0 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[5-(1H-benzimidazol-2-yl)pentyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

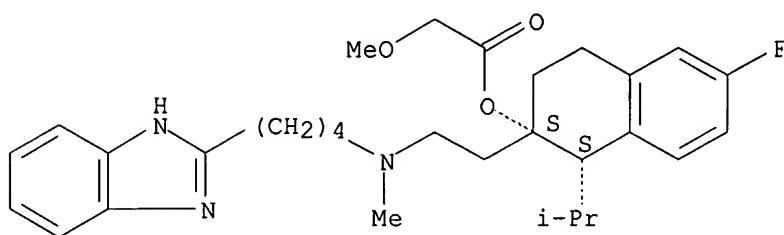


● 2 HCl

RN 116666-76-3 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[4-(1H-benzimidazol-2-yl)butyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, (1S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

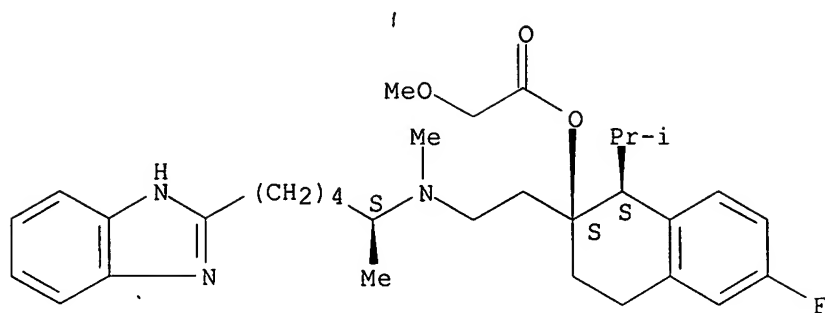


● 2 HCl

RN 116666-93-4 HCAPLUS

CN Acetic acid, methoxy-, 2-[2-[[5-(1H-benzimidazol-2-yl)-1-methylpentyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride, [1S-[1 α ,2 α ,2(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

=> d que stat 141

L31 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116644-53-2
 L41 416 SEA FILE=HCAPLUS ABB=ON PLU=ON L31

=> d 141 ibib hitstr 1-5 400-416

L41 ANSWER 1 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:107381 HCAPLUS

DOCUMENT NUMBER: 144:121407

TITLE: Relaxant responses to calcium channel antagonists and potassium channel opener in human saphenous vein

AUTHOR(S): Ford, C.; Bieger, D.; Mong, K.; Tabrizchi, R.

CORPORATE SOURCE: Division of Basic Medical Sciences, Faculty of Medicine, Health Sciences Centre, Memorial University of Newfoundland, St John's, NL, A1B 3V6, Can.

SOURCE: Autonomic & Autacoid Pharmacology (2006), 26(1), 7-13
 CODEN: AAPUC3; ISSN: 1474-8665

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

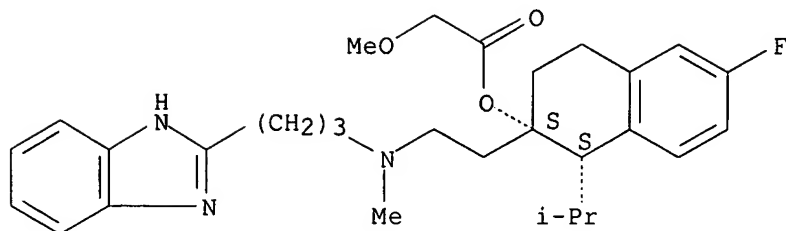
IT 116644-53-2, Mibefradil

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (relaxant responses to calcium channel antagonists and potassium channel opener in human saphenous vein)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:100738 HCAPLUS

DOCUMENT NUMBER: 144:198849

TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients

INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar

PATENT ASSIGNEE(S): India

SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024365	A1	20060202	US 2005-134633	20050519
US 2004096499	A1	20040520	US 2003-630446	20030729
PRIORITY APPLN. INFO.:			IN 2002-MU697	A 20020805
			IN 2002-MU699	A 20020805
			IN 2003-MU80	A 20030122
			IN 2003-MU82	A 20030122
			US 2003-630446	A2 20030729

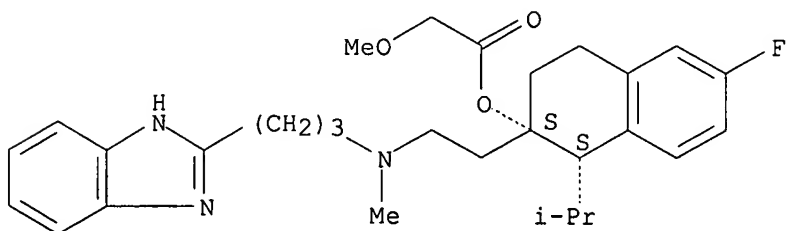
IT 116644-53-2, Mibefradil

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

RN 116644-53-2 HCAPLUS

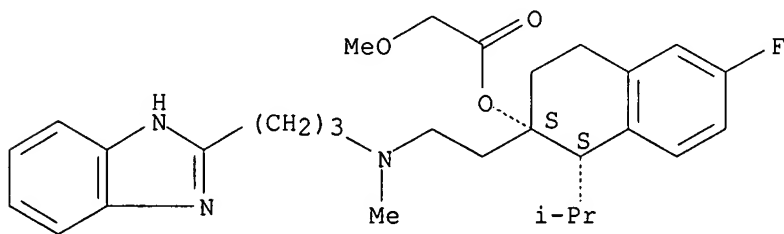
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 3 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:56562 HCAPLUS
DOCUMENT NUMBER: 144:246907
TITLE: Inhibitory Effect of Efonidipine on Aldosterone
Synthesis and Secretion in Human Adrenocarcinoma
(H295R) Cells
AUTHOR(S): Imagawa, Keiichi; Okayama, Satoshi; Takaoka, Minoru;
Kawata, Hiroyuki; Naya, Noriyuki; Nakajima, Tamio;
Horii, Manabu; Uemura, Shiro; Saito, Yoshihiko
CORPORATE SOURCE: First Department of Internal Medicine, Nara Medical
University, Kashihara, Nara, Japan
SOURCE: Journal of Cardiovascular Pharmacology (2006), 47(1),
133-138
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116644-53-2, Mibefradil
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitory effect of efonidipine on aldosterone synthesis and
secretion in human adrenocarcinoma cells)
RN 116644-53-2 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-
2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 4 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:51871 HCAPLUS
DOCUMENT NUMBER: 144:121827
TITLE: Methods for preventing pressure-induced apoptotic
neural-cell death in glaucoma patients by
administering inhibitors of TREK-1 and TRAAK potassium
channels
INVENTOR(S): Coroneo, Minas Theodore
PATENT ASSIGNEE(S): Davies Collison Cave, Australia
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S.
Ser. No. 84,604.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006013814	A1	20060119	US 2005-171531	20050630
US 2002187919	A1	20021212	US 2002-84604	20020227
PRIORITY APPLN. INFO.:			US 2000-649643	B1 20000829
			US 2002-84604	B2 20020227
			AU 2000-9267	A 20000808

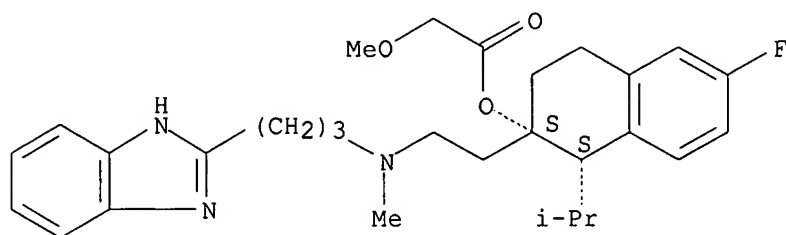
IT 116644-53-2, Mibefradil

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods for preventing pressure-induced apoptotic neural-cell death in glaucoma patients by administering inhibitors of TREK-1 and TRAAK potassium channels)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 5 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:5456 HCAPLUS

DOCUMENT NUMBER: 144:205445

TITLE: Antihypertensive Effects of the Putative T-Type Calcium Channel Antagonist Mibefradil Are Mediated by the L-Type Calcium Channel Cav1.2

AUTHOR(S): Moosmang, Sven; Haider, Nicole; Bruederl, Birgit; Welling, Andrea; Hofmann, Franz

CORPORATE SOURCE: Institut fuer Pharmakologie und Toxikologie, Technische Universitaet Muenchen, Germany

SOURCE: Circulation Research (2006), 98(1), 105-110
 CODEN: CIRUAL; ISSN: 0009-7330

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

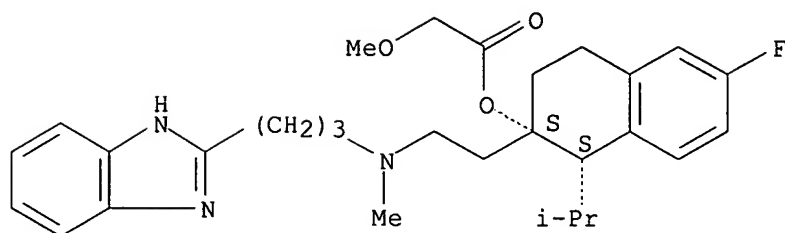
IT 116644-53-2, Mibefradil

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihypertensive effects of the putative T-type calcium channel antagonist mibefradil are mediated by the L-type calcium channel Cav1.2)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

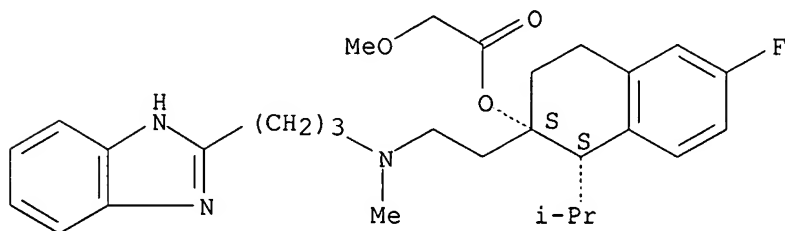
Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 400 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:263166 HCAPLUS
 DOCUMENT NUMBER: 124:332465
 TITLE: Effect of mibefradil on left ventricular diastolic function in patients with congestive heart failure
 AUTHOR(S): Muntinga, H. J.; van der Vring, J. A. F. M.; Niemeyer, M. G.; van den Berg, F.; Knol, H. R.; Bernink, P. J. L. M.; van der Wall, E. E.; Blanksma, P. K.; Lie, K. I.
 CORPORATE SOURCE: Dep. Cardiology, Martini Hospital, Groningen, 9700 RM, Neth.
 SOURCE: Journal of Cardiovascular Pharmacology (1996), 27(5), 652-6
 CODEN: JPCPDT; ISSN: 0160-2446
 PUBLISHER: Lippincott-Raven
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of mibefradil on left ventricular diastolic function in patients with congestive heart failure)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

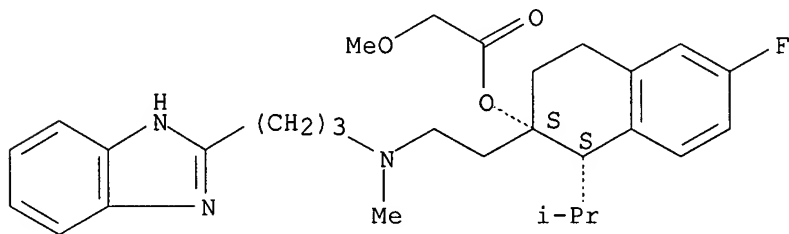
Absolute stereochemistry.



L41 ANSWER 401 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:205846 HCAPLUS
 DOCUMENT NUMBER: 124:278618
 TITLE: Antihypertensive properties of the novel calcium antagonist mibefradil (Ro 40-5967): A new generation

of calcium antagonists?
 AUTHOR(S): Bernink, Peter J. L. M.; Prager, Gerold; Schelling, Arie; Kobrin, Isaac
 CORPORATE SOURCE: Martini Ziekenhuis, Groningen, 9721 5W, Neth.
 SOURCE: Hypertension (Dallas) (1996), 27(3, Pt. 1), 426-32
 CODEN: HPRTDN; ISSN: 0194-911X
 PUBLISHER: American Heart Association
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihypertensive properties of the novel calcium antagonist mibefradil (Ro 40-5967): a new generation of calcium antagonists)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

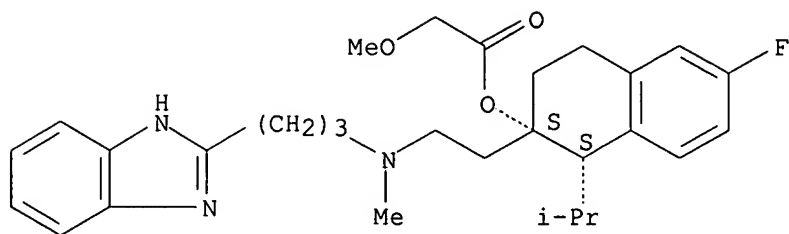
Absolute stereochemistry.



L41 ANSWER 402 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:138785 HCAPLUS
 DOCUMENT NUMBER: 124:250257
 TITLE: Effects of a new calcium antagonist, mibefradil (Ro 40-5967), on silent ischemia in patients with stable chronic angina pectoris: A multicenter placebo-controlled study
 AUTHOR(S): Braun, Shimon; Van Der Wall, Ernst E.; Emanuelsson, Haken; Kobrin, Isaak
 CORPORATE SOURCE: Department Cardiology, Tel-Aviv Medical Center, Tel Aviv-Jaffa, 64239, Israel
 SOURCE: Journal of the American College of Cardiology (1996), 27(2), 317-22
 CODEN: JACCDI; ISSN: 0735-1097
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of a new calcium antagonist, mibefradil (Ro 40-5967), on silent ischemia in human patients with stable chronic angina pectoris)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 403 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:115986 HCAPLUS

DOCUMENT NUMBER: 124:219315

TITLE: Hemodynamics, cardiac conduction and pharmacokinetics of mibefradil (Ro 40-5967), a novel calcium antagonist

AUTHOR(S): Petrie, John R.; Glen, Stephen K.; MacMahon, Mark; Crome, Renata; Meredith, Peter A.; Elliott, Henry L.; Reid, John L.

CORPORATE SOURCE: Department Medicine and Therapeutics, Western Infirmary, Glasgow, G11 6NT, UK

SOURCE: Journal of Hypertension (1995), 13(12, Pt. 2), 1842-6
CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Current Science

DOCUMENT TYPE: Journal

LANGUAGE: English

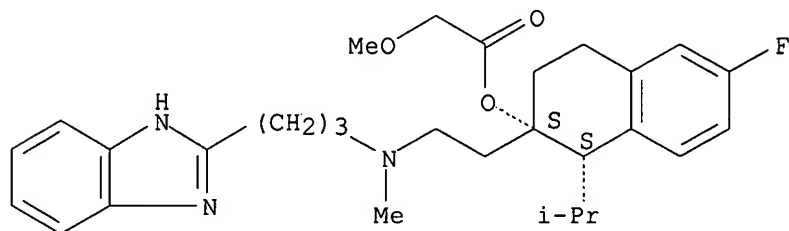
IT 116644-53-2, Mibefradil

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hemodynamics, cardiac conduction and pharmacokinetics of mibefradil (Ro 40-5967), a novel calcium antagonist, in humans)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 404 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

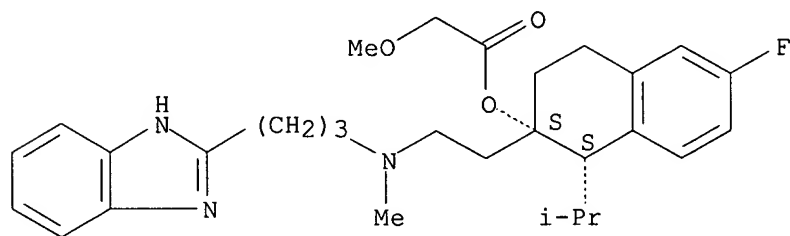
ACCESSION NUMBER: 1996:36342 HCAPLUS

DOCUMENT NUMBER: 124:135217

TITLE: Effects of mibefradil on intracellular Ca²⁺ release in cultured rat cardiac fibroblasts and human platelets

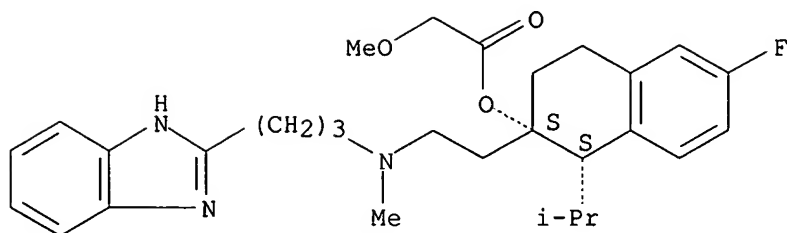
AUTHOR(S): Eberhard, Marc; Miyagawa, Koichi; Hermsmeyer, Kent; Erne, Paul
 CORPORATE SOURCE: Dep. Res., Kantonsspital, Basel, CH-4031, Switz.
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1995), 353(1), 94-101
 CODEN: NSAPCC; ISSN: 0028-1298
 PUBLISHER: Springer
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (mibefradil effect on calcium release in cardiac fibroblasts and human platelets)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



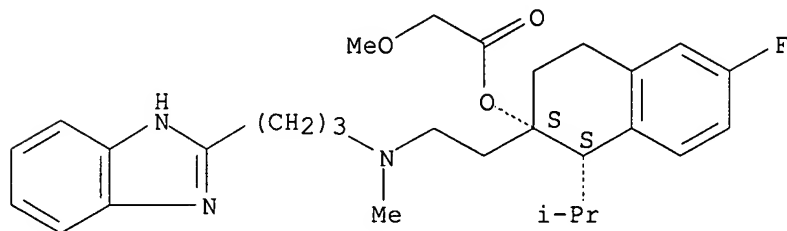
L41 ANSWER 405 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:31775 HCAPLUS
 DOCUMENT NUMBER: 124:44687
 TITLE: Nonlinear Pharmacokinetics of Mibefradil in the Dog
 AUTHOR(S): Skerjanec, Andrej; Tawfik, Soheir; Tam, Yun K.
 CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, T6G 2N8, Can.
 SOURCE: Journal of Pharmaceutical Sciences (1996), 85(2), 189-92
 CODEN: JPMSAE; ISSN: 0022-3549
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (nonlinear pharmacokinetics of mibefradil in the dog)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 406 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:29294 HCAPLUS
 DOCUMENT NUMBER: 124:105447
 TITLE: Two stable cell lines for screening of calcium channel blockers
 AUTHOR(S): Seisenberger, Claudia; Welling, Andrea; Schuster, Angela; Hofmann, Franz
 CORPORATE SOURCE: Inst. Pharmakologie und Toxikologie, TU Muenchen, Munich, D-80802, Germany
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1995), 352(6), 662-9
 CODEN: NSAPCC; ISSN: 0028-1298
 PUBLISHER: Springer
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (two stable cell lines for screening of calcium channel blockers)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

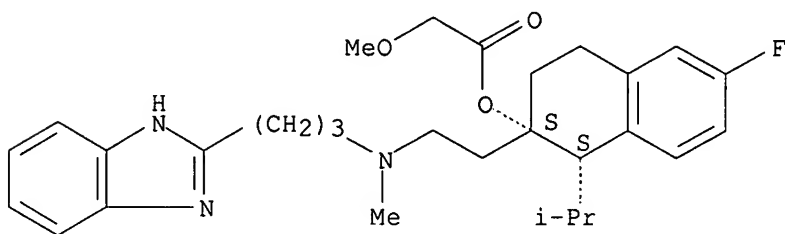
Absolute stereochemistry.



L41 ANSWER 407 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1996:28720 HCAPLUS
 DOCUMENT NUMBER: 124:106113
 TITLE: Mechanism of the antiischemic effect of mibefradil, a selective T calcium channel blocker in dogs: comparison with amlodipine
 AUTHOR(S): Roux, Sebastien; Buehler, Manfred; Clozel, Jean-Paul
 CORPORATE SOURCE: Pharma Division, F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
 SOURCE: Journal of Cardiovascular Pharmacology (1996), 27(1), 132-9

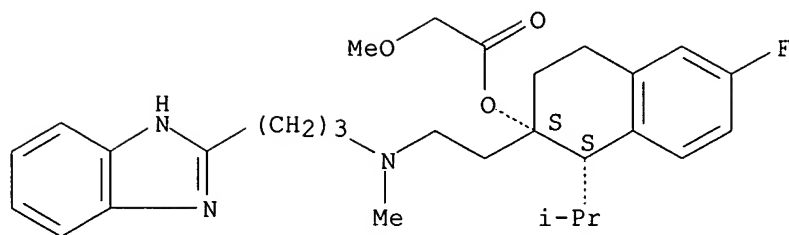
CODEN: JPCPDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116644-53-2, Mibefradil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of the antiischemic effect of mibefradil, a selective T calcium channel blocker in dogs: comparison with amlodipine)
RN 116644-53-2 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



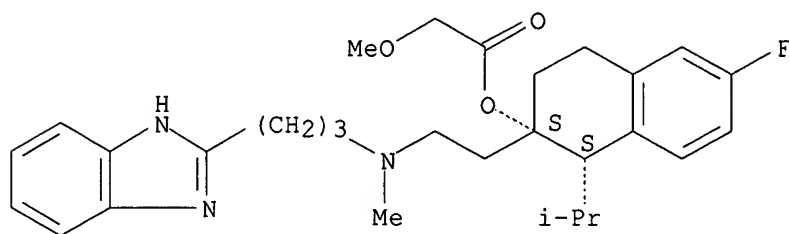
L41 ANSWER 408 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:941601 HCAPLUS
DOCUMENT NUMBER: 124:52435
TITLE: Structural changes and cyclic GMP content of the aorta after calcium antagonism or angiotensin converting enzyme inhibition in renovascular hypertensive rats
AUTHOR(S): Veniant, Murielle; Gray, Gillian A.; Heudes, Didier; Menard, Joel; Clozel, Jean-Paul
CORPORATE SOURCE: Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd, Basel, Switz.
SOURCE: Journal of Hypertension (1995), 13(7), 731-7
CODEN: JOHYD3; ISSN: 0263-6352
PUBLISHER: Current Science
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116644-53-2, Mibefradil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cGMP content and structural changes of aorta after calcium antagonism or angiotensin converting enzyme inhibition in renovascular hypertensive rats)
RN 116644-53-2 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 409 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:911235 HCAPLUS
 DOCUMENT NUMBER: 124:21374
 TITLE: Effects of the new calcium antagonist mibefradil (Ro 40-5967) on exercise duration in patients with chronic stable angina pectoris: A multicenter, placebo-controlled study
 AUTHOR(S): Bakx, Ad L. M.; van der Wall, Ernst E.; Braun, Shimon; Emanuelsson, Hakan; Bruschke, Albert V. G.; Kobrin, Isaac
 CORPORATE SOURCE: University Hospital, Leiden, Neth.
 SOURCE: American Heart Journal (1995), 130(4), 748-57
 CODEN: AHJOA2; ISSN: 0002-8703
 PUBLISHER: Mosby-Year Book
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of the new calcium antagonist mibefradil (Ro 40-5967) on exercise duration in human patients with chronic stable angina pectoris)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 410 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:865388 HCAPLUS
 DOCUMENT NUMBER: 123:329616
 TITLE: The block of the expressed L-type calcium channel is modulated by the $\beta 3$ subunit
 AUTHOR(S): Lacinova, L.; Ludwig, A.; Bosse, E.; Flockerzi, V.; Hofmann, F.

CORPORATE SOURCE: Institut fuer Pharmakologie and Toxikologie TU
Muenchen, Biedersteiner Str. 29, 80802, Munchen,
Germany

SOURCE: FEBS Letters (1995), 373(2), 103-7
CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

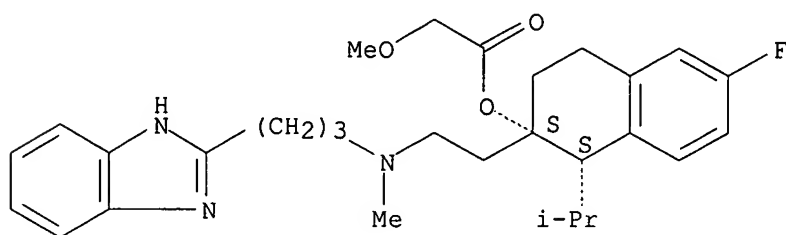
LANGUAGE: English

IT 116644-53-2, Mibefradil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(block of the expressed L-type calcium channel is modulated by the $\beta 3$ subunit)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 411 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:846309 HCAPLUS

DOCUMENT NUMBER: 123:275587

TITLE: Voltage-dependent blockade of diverse types of voltage-gated Ca^{2+} channels expressed in *Xenopus* oocytes by the Ca^{2+} channel antagonist mibefradil (Ro 40-5967)

AUTHOR(S): Bezprozvanny, I.; Tsien, R. W.

CORPORATE SOURCE: Dep. Mol. Cellular Physiology, Stanford University
Medical Center, Stanford, CA, 94305, USA

SOURCE: Molecular Pharmacology (1995), 48(3), 540-9
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

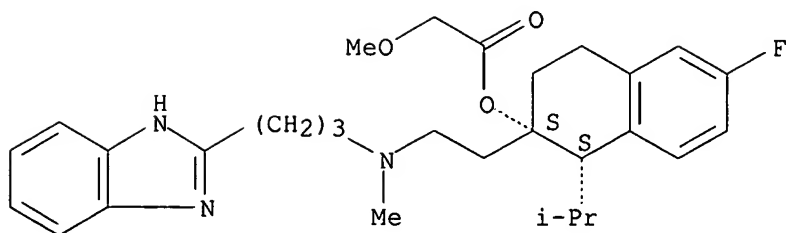
LANGUAGE: English

IT 116644-53-2, Mibefradil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(voltage-dependent blockade of diverse types of voltage-gated Ca^{2+} channels expressed in *Xenopus* oocytes by mibefradil)

RN 116644-53-2 HCAPLUS

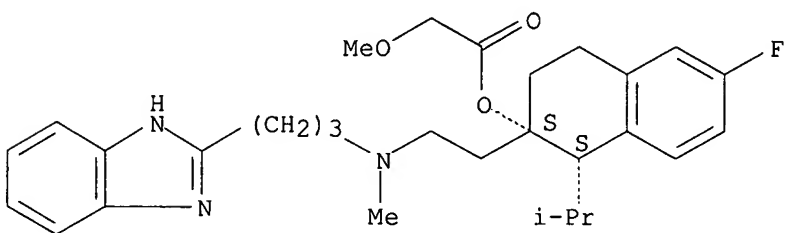
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 412 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:755107 HCAPLUS
 DOCUMENT NUMBER: 123:188106
 TITLE: Mibefradil prevents neointima formation after vascular injury in rats: possible role of the blockade of the T-type voltage-operated calcium channel
 AUTHOR(S): Schmitt, R.; Clozel, J.-P.; Iberg, N.; Buehler, F. R.
 CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
 SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (1995), 15(8), 1161-5
 CODEN: ATVBFA; ISSN: 1079-5642
 PUBLISHER: American Heart Association
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (role of calcium T-channels in blockade of injury-induced artery neointima formation by mibefradil)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

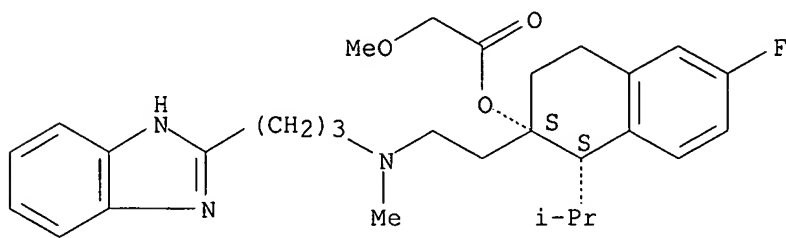
Absolute stereochemistry.



L41 ANSWER 413 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:719615 HCAPLUS
 DOCUMENT NUMBER: 123:132462
 TITLE: Differential effects of the calcium antagonist mibefradil in epicardial and intramyocardial coronary arteries
 AUTHOR(S): Kueng, Christoph F.; Tschudi, Marcel R.; Noll, Georg;
 Clozel, Jean-Paul; Luescher, Thomas F.
 CORPORATE SOURCE: Department of Research, University Hospital, Basel, Switz.

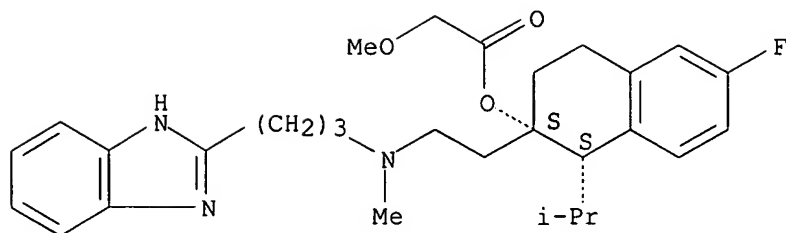
SOURCE: Journal of Cardiovascular Pharmacology (1995), 26(2), 312-18
 CODEN: JCPCDT; ISSN: 0160-2446
 PUBLISHER: Lippincott-Raven
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (calcium antagonist mibefradil effects in epicardial and intramyocardial coronary arteries)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



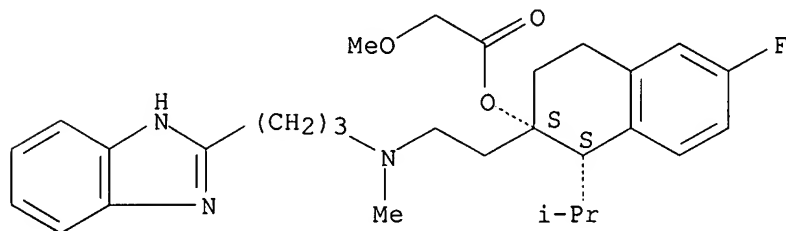
L41 ANSWER 414 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:714882 HCAPLUS
 DOCUMENT NUMBER: 123:101913
 TITLE: High-performance liquid chromatographic analysis of mibefradil in dog plasma and urine
 AUTHOR(S): Skerjanec, A.; Tam, Y. K.
 CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, T6G 2N8, Can.
 SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 669(2), 377-82
 CODEN: JCBBEF; ISSN: 0378-4347
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 116644-53-2, Mibefradil
 RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 (mibefradil determination in plasma and urine by HPLC)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 415 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1993:15784 HCAPLUS
 DOCUMENT NUMBER: 118:15784
 TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway
 AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.; Kozlowski, U. M.; Worth, E.
 CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK
 SOURCE: Xenobiotica (1992), 22(7), 837-57
 CODEN: XENOBH; ISSN: 0049-8254
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT **116644-53-2**
 RL: PROC (Process)
 (as Ro 5967 metabolite, characterization of, by diode-array UV spectroscopy and thermospray-mass spectrometry)
 RN 116644-53-2 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L41 ANSWER 416 OF 416 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1988:549535 HCAPLUS
 DOCUMENT NUMBER: 109:149535
 TITLE: Preparation of [(heterocyclalalkyl)amino]ethyl]tetrahydronaphthalenes as cardiovascular agents
 INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerki, Hans Peter; Marti, Fraenzi; Ramuz, Henri
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 37 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent

LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8705599	A	19880515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		
PRIORITY APPLN. INFO.:			CH 1986-4565	A 19861114
			EP 1987-116251	A 19871104

OTHER SOURCE(S): MARPAT 109:149535

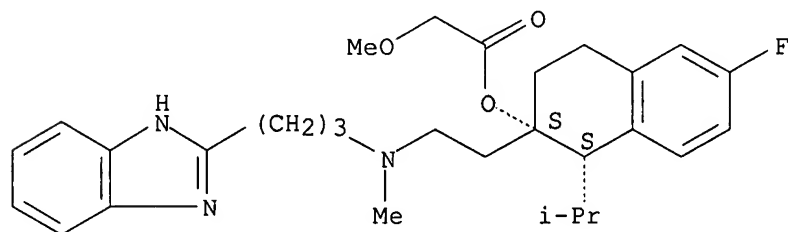
IT 116644-53-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as cardiovascular agent)

RN 116644-53-2 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d que stat 142

L38 1 SEA FILE=REGISTRY ABB=ON PLU=ON 116666-63-8
 142 63 SEA FILE=HCAPLUS ABB=ON PLU=ON L38

=> d 142 ibib hitstr 1-5 50-63

L42 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:100738 HCAPLUS

DOCUMENT NUMBER: 144:198849

TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients

INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar

PATENT ASSIGNEE(S): India

SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024365	A1	20060202	US 2005-134633	20050519
US 2004096499	A1	20040520	US 2003-630446	20030729
PRIORITY APPLN. INFO.:			IN 2002-MU697	A 20020805
			IN 2002-MU699	A 20020805
			IN 2003-MU80	A 20030122
			IN 2003-MU82	A 20030122
			US 2003-630446	A2 20030729

IT 116666-63-8, Mibefradil dihydrochloride

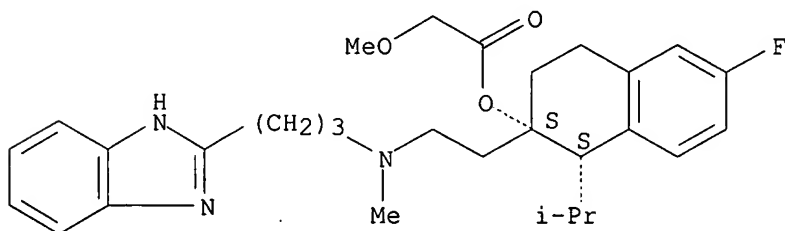
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel dosage form comprising modified-release and immediate-release active ingredients)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1335082 HCAPLUS
 DOCUMENT NUMBER: 144:57599
 TITLE: Transdermal delivery system for statin combination therapy
 INVENTOR(S): Lane, Edward M.
 PATENT ASSIGNEE(S): Fairfield Clinical Trials, LLC, USA
 SOURCE: U.S. Pat. Appl. Publ., 7 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005281868	A1	20051222	US 2005-156744	20050621
WO 2006002127	A1	20060105	WO 2005-US21855	20050621

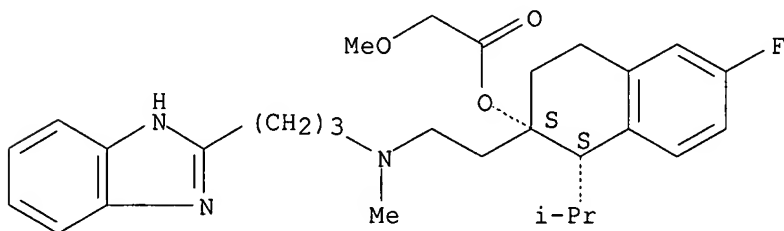
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-580734P P 20040621
 US 2004-612828P P 20040927

IT 116666-63-8, Posicor
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (transdermal delivery system for statin combination therapy of lipid disorders)
 RN 116666-63-8 HCAPLUS
 CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

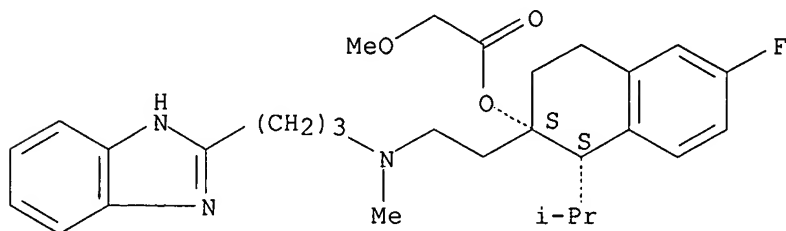
Absolute stereochemistry.



● 2 HCl

L42 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:388287 HCAPLUS
DOCUMENT NUMBER: 143:71181
TITLE: Modulation of Oral Squamous Cell Carcinoma Incidence
in Rats Via Diet and a Novel Calcium Channel
Antagonist
AUTHOR(S): Lenz, Barbara; Cramer, Flavio M.; Eichler, David A.;
Schlaeppli, Bernhard; Wiltshire, Hugh R.; Wood, John;
Seymour, Robin A.
CORPORATE SOURCE: Non-Clinical Development-Drug Safety, Hoffmann-La
Roche Ltd., Basel, Switz.
SOURCE: Toxicologic Pathology (2005), 33(3), 356-364
CODEN: TOPADD; ISSN: 0192-6233
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8, Mibefradil dihydrochloride
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of
action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(mibefradil dihydrochloride showed dose dependent gingival overgrowth
in incisor and molar teeth independent of diet used, high-dose
administration raised incidence of periodontitis and squamous cell
carcinoma in rat)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-
2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:292562 HCAPLUS
DOCUMENT NUMBER: 140:399350
TITLE: NNC 55-0396 [(1S,2S)-2-(2-(N-[(3-benzimidazol-2-
yl)propyl]-N-methylamino)ethyl)-6-fluoro-1,2,3,4-
tetrahydro-1-isopropyl-2-naphthyl
cyclopropanecarboxylate dihydrochloride]: a new
selective inhibitor of T-type calcium channels
AUTHOR(S): Huang, Luping; Keyser, Brian M.; Tagmose, Tina M.;
Hansen, J. Bondo; Taylor, James T.; Zhuang, Hean;

CORPORATE SOURCE: Zhang, Min; Ragsdale, David S.; Li, Ming
 Department of Pharmacology, Tulane University Health
 Sciences Center, New Orleans, LA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics
 (2004), 309(1), 193-199
 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental
 Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

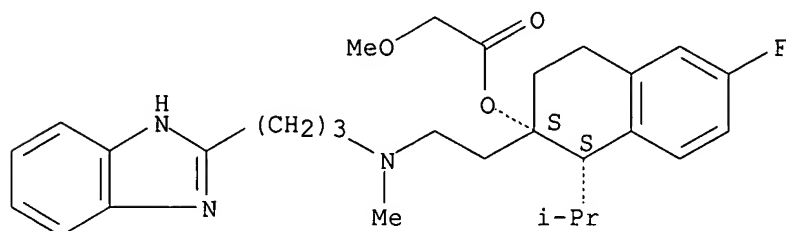
OTHER SOURCE(S): CASREACT 140:399350

IT **116666-63-8**, Mibefradil dihydrochloride
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (mibefradil derivative selectively inhibits T-type calcium channels)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-
 2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:916407 HCAPLUS

DOCUMENT NUMBER: 136:53755

TITLE: Synthesis of nitrosated and nitrosylated
 (hetero)cyclic phosphodiesterase inhibitors used in
 treatment of sexual dysfunction

INVENTOR(S): Garvey, David S.; Saenz de Tejada, Inigo; Earl,
 Richard A.; Khanapure, Subhash P.

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: U.S., 117 pp., Cont.-in-part of U.S. 5,958,926.
 CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6331543	B1	20011218	US 1999-387727	19990901
US 5874437	A	19990223	US 1996-740764	19961101

WO 9819672 A1 19980514 WO 1997-US19870 19971031
 W: AU, CA, JP, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 US 5958926 A 19990928 US 1998-145142 19980901
 US 2002019405 A1 20020214 US 2001-941691 20010830
 US 6462044 B2 20021008
 US 2003023087 A1 20030130 US 2002-216886 20020813
 US 6930113 B2 20050816
 US 2004087591 A1 20040506 US 2003-694183 20031028
 PRIORITY APPLN. INFO.: US 1996-740764 A2 19961101
 WO 1997-US19870 A2 19971031
 US 1998-145142 A2 19980901
 US 1999-387727 A1 19990901
 US 2001-941691 A3 20010830
 US 2002-216866 A3 20020813

OTHER SOURCE(S): MARPAT 136:53755

IT 116666-63-8D, Posicor, nitroso derivs.

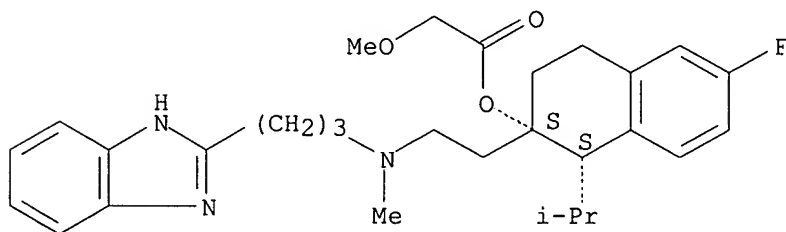
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(synthesis of nitrosated and nitrosylated (hetero)cyclic
 phosphodiesterase inhibitors used in treatment of sexual dysfunction)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
 yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-
 2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 50 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:204998 HCAPLUS

DOCUMENT NUMBER: 118:204998

TITLE: Effects of Ro 40-5967, a new calcium antagonist, and
 enalapril on cardiac remodeling in renal hypertensive
 rats

AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Heudes, Didier;
 Banken, Ludger; Menard, Joel

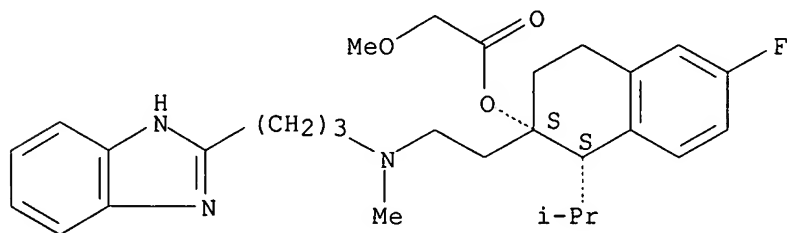
CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche, Basel, CH-4002,
 Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1993), 21(4),
 544-51

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal
LANGUAGE: English
IT **116666-63-8**
RL: BIOL (Biological study)
(cardiac remodeling in renal hypertension response to enalapril vs.)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

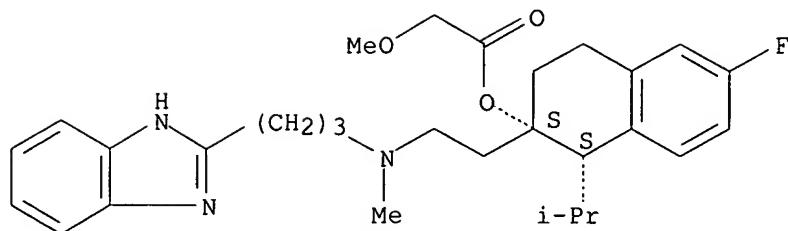
Absolute stereochemistry.



● 2 HCl

L42 ANSWER 51 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:139549 HCAPLUS
DOCUMENT NUMBER: 118:139549
TITLE: Ro 40-5967, a novel calcium channel antagonist, protects against ventricular fibrillation
AUTHOR(S): Billman, George E.
CORPORATE SOURCE: Dep. Physiol., Ohio State Univ., Columbus, OH, USA
SOURCE: European Journal of Pharmacology (1993), 229(2-3), 179-87
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **116666-63-8**
RL: PRP (Properties)
(antiarrhythmic effects of, in heart ischemia and ventricular fibrillation)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:15784 HCAPLUS

DOCUMENT NUMBER: 118:15784

TITLE: Metabolism of calcium antagonist Ro 40-5967: a case history of the use of diode-array UV spectroscopy and thermospray-mass spectrometry in the elucidation of a complex metabolic pathway

AUTHOR(S): Wiltshire, H. R.; Harris, S. R.; Prior, K. J.;

Kozlowski, U. M.; Worth, E.

CORPORATE SOURCE: Dep. Pharmacokinet. Metab., Roche Prod. Ltd., Welwyn Garden City/Herts., AL7 3AY, UK

SOURCE: Xenobiotica (1992), 22(7), 837-57

CODEN: XENOBH; ISSN: 0049-8254

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 116666-63-8

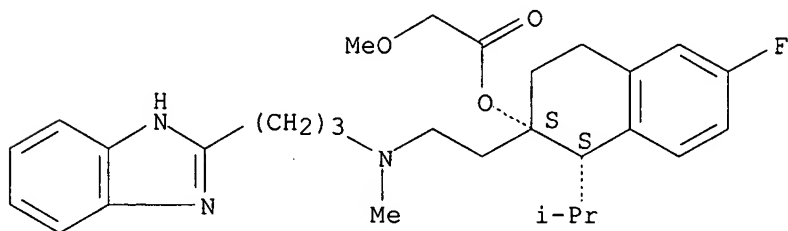
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolism of, diode-array UV spectroscopy and thermospray-mass spectrometry in elucidation of complex metabolic pathway in)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

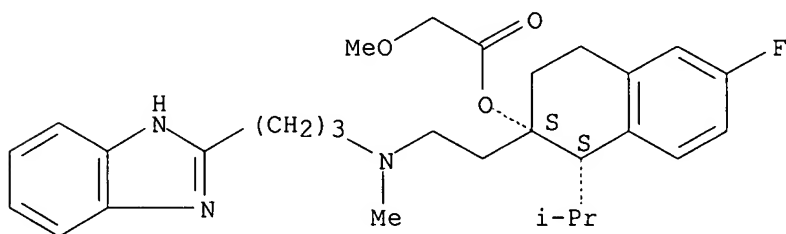
Absolute stereochemistry.



● 2 HCl

L42 ANSWER 53 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:604926 HCAPLUS
DOCUMENT NUMBER: 117:204926
TITLE: Effect of calcium channel antagonists on the cardiac
vagal tone response to submaximal exercise
AUTHOR(S): Billman, George E.; Halliwill, John R.; Avendano,
Christopher E.
CORPORATE SOURCE: Dep. Physiol., Ohio State Univ., Columbus, OH, USA
SOURCE: Drug Development Research (1992), 27(2), 89-106
CODEN: DDREDK; ISSN: 0272-4391
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: BIOL (Biological study)
(exercise effect on cardiac vagal tone response to, as calcium channel
antagonist)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-
2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

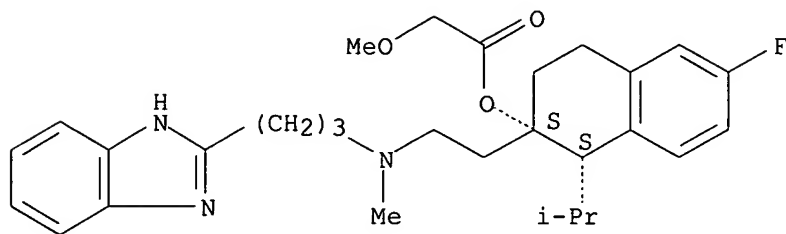


● 2 HCl

L42 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:143594 HCAPLUS
DOCUMENT NUMBER: 116:143594
TITLE: Hemodynamic profile of Ro 40-5967 in conscious rats:
comparison with diltiazem, verapamil, and amlodipine
AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Hess, Patrick;
Wolfgang, Robert
CORPORATE SOURCE: Pharma Div., F. Hoffmann-La Roche Ltd., Basel,
CH-4002, Switz.
SOURCE: Journal of Cardiovascular Pharmacology (1991),
18(Suppl. 10), S55-S58
CODEN: JPCPDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: BIOL (Biological study)
(hemodynamic profile of, as calcium antagonist)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-
yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:33723 HCAPLUS

DOCUMENT NUMBER: 116:33723

TITLE: Ro 40-5967: a new nondihydropyridine calcium antagonist

AUTHOR(S): Clozel, Jean Paul; Osterrieder, Wolfgang; Kleinbloesem, Cornelis H.; Welker, Horst A.; Schlaeppli, Bernhard; Tudor, Robert; Hefti, Fridolin; Schmitt, Rita; Eggers, Herwig

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.

SOURCE: Cardiovascular Drug Reviews (1991), 9(1), 4-17

CODEN: CDREEA; ISSN: 0897-5957

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

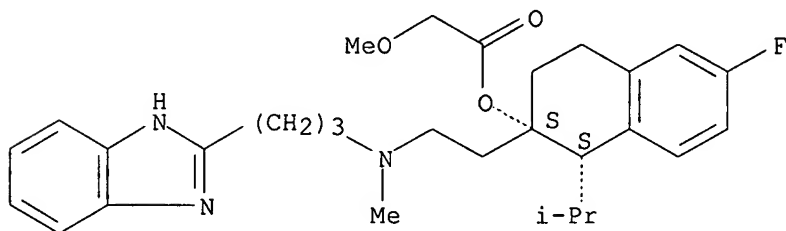
IT 116666-63-8

RL: BIOL (Biological study)
(as nondihydropyridine calcium antagonist)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

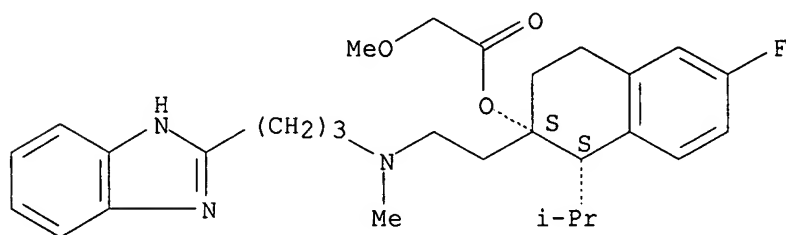
Absolute stereochemistry.



● 2 HCl

L42 ANSWER 56 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:240328 HCAPLUS
DOCUMENT NUMBER: 114:240328
TITLE: Potential-dependent inhibition of cardiac calcium inward currents by Ro 40-5967 and verapamil: relation to negative inotropy
AUTHOR(S): Fang, Liang Min; Osterrieder, Wolfgang
CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
SOURCE: European Journal of Pharmacology (1991), 196(2), 205-7
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: BIOL (Biological study)
(heart calcium currents and neg. inotropic response to)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

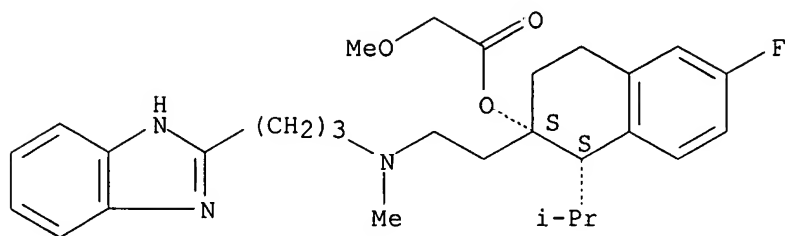


● 2 HCl

L42 ANSWER 57 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:240319 HCAPLUS
DOCUMENT NUMBER: 114:240319
TITLE: Increased negative inotropic effect of calcium-channel blockers in hypertrophied and failing rabbit heart
AUTHOR(S): Ezzaher, Abdellatif; Bouanani, Nour el Houda; Su, Jin Bo; Hittinger, Luc; Crozatier, Bertrand
CORPORATE SOURCE: Fac. Med., Hop. Henri Mondor, Creteil, 94000, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1991), 257(1), 466-71
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: PRP (Properties)
(increased neg. inotropic effect of, in heart failure and hypertrophy)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-

2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:94918 HCAPLUS

DOCUMENT NUMBER: 114:94918

TITLE: Ro 40-5967, in contrast to diltiazem, does not reduce left ventricular contractility in rats with chronic myocardial infarction

AUTHOR(S): Veniant, Murielle; Clozel, Jean Paul; Hess, Patrick; Wolfgang, Robert

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffman-La Roche Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1991), 17(2), 277-84

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 116666-63-8, Ro 40-5967

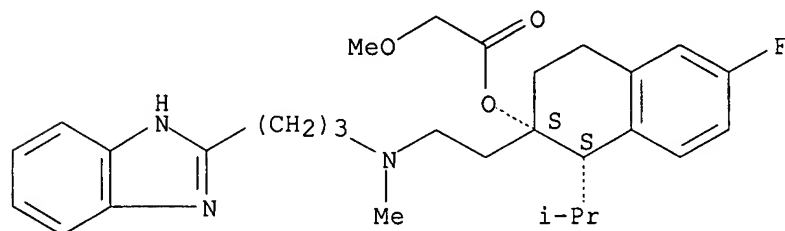
RL: PRP (Properties)

(neg. inotropic effect of, in heart infarction)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

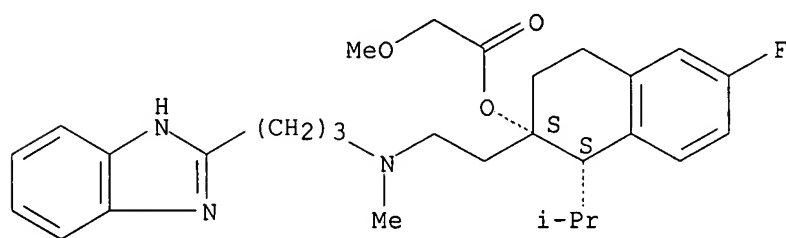
Absolute stereochemistry.



● 2 HCl

L42 ANSWER 59 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:609229 HCAPLUS
DOCUMENT NUMBER: 113:209229
TITLE: The proliferative response to vascular injury is suppressed by angiotensin-converting enzyme inhibition
AUTHOR(S): Powell, Jerry S.; Mueller, Rita K. M.; Rouge, Marianne; Kuhn, Herbert; Hefti, Fridolin; Baumgartner, Hans R.
CORPORATE SOURCE: F. Hoffmann-La Roche Ltd., Basel, Switz.
SOURCE: Journal of Cardiovascular Pharmacology (1990), 16(Suppl. 4), S42-S49
CODEN: JPCPDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: BIOL (Biological study)
(blood vessel proliferation response to, angiotensin-converting enzyme inhibition in relation to)
RN 116666-63-8 HCAPLUS
CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:229520 HCAPLUS
DOCUMENT NUMBER: 112:229520
TITLE: Antihypertensive properties of the novel calcium antagonist (1S,2S)-2-[2-[[3-(2-benzimidazolyl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthyl methoxyacetate dihydrochloride in rat models of hypertension. Comparison with verapamil
AUTHOR(S): Hefti, F.; Clozel, J. P.; Osterrieder, W.
CORPORATE SOURCE: F. Hoffmann-La Roche Ltd., Basel, Switz.
SOURCE: Arzneimittel-Forschung (1990), 40(4), 417-21
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 116666-63-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

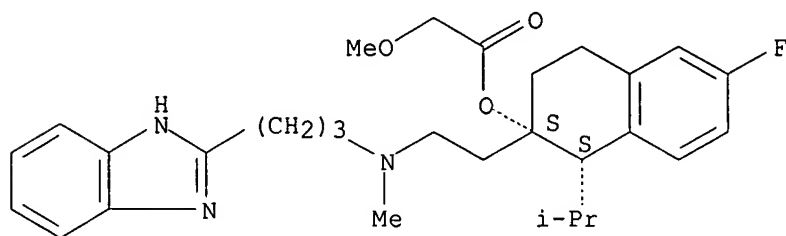
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antihypertensive activity of)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:625064 HCAPLUS

DOCUMENT NUMBER: 111:225064

TITLE: Effects of Ro 40-5967, a novel calcium antagonist, on myocardial function during ischemia induced by lowering coronary perfusion pressure in dogs: comparison with verapamil

AUTHOR(S): Clozel, Jean Paul; Banken, Ludger; Osterrieder, Wolfgang

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1989), 14(5), 713-21

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal

LANGUAGE: English

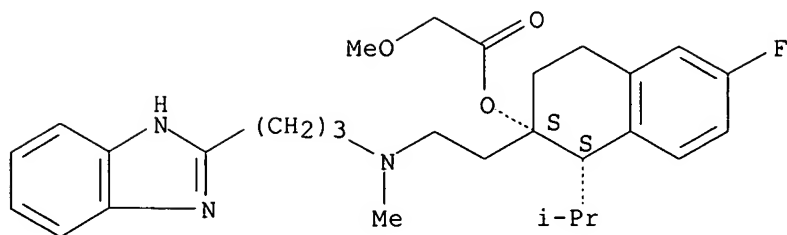
IT 116666-63-8, Ro 40-5967

RL: BIOL (Biological study)
(heart ischemia inhibition by)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:400442 HCAPLUS

DOCUMENT NUMBER: 111:442

TITLE: In vitro pharmacologic profile of Ro 40-5967, a novel calcium channel blocker with potent vasodilator but weak inotropic action

AUTHOR(S): Osterrieder, Wolfgang; Holck, Mark

CORPORATE SOURCE: Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Cardiovascular Pharmacology (1989), 13(5), 754-9

CODEN: JCPCDT; ISSN: 0160-2446

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 116666-63-8, Ro 40-5967

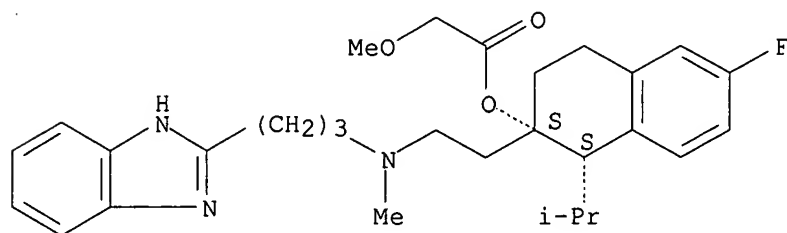
RL: BIOL (Biological study)

(coronary artery dilation by, inotropic action in relation to)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L42 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:549535 HCAPLUS

DOCUMENT NUMBER: 109:149535

TITLE: Preparation of [[(heterocyclalkyl)amino]ethyl]tetrahydro-
naphthalenes as cardiovascular agents
INVENTOR(S): Branca, Quirico; Jaunin, Roland; Maerki, Hans Peter;
Marti, Fraenzi; Ramuz, Henri
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 268148	A1	19880525	EP 1987-116251	19871104
EP 268148	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8705599	A	19880515	DK 1987-5599	19871026
DK 171349	B1	19960916		
CA 1319144	A1	19930615	CA 1987-550190	19871026
CS 264350	B2	19890712	CS 1987-7874	19871103
AT 70267	E	19911215	AT 1987-116251	19871104
ES 2040234	T3	19931016	ES 1987-116251	19871104
ZA 8708362	A	19880727	ZA 1987-8362	19871106
AU 8780909	A1	19880519	AU 1987-80909	19871109
AU 600769	B2	19900823		
IL 84407	A1	19910916	IL 1987-84407	19871109
JP 63139171	A2	19880610	JP 1987-282287	19871110
JP 2504490	B2	19960605		
US 4808605	A	19890228	US 1987-119114	19871110
HU 60251	A2	19920828	HU 1987-5011	19871111
HU 215915	B	19990329		
FI 8705024	A	19880515	FI 1987-5024	19871113
FI 94414	B	19950531		
FI 94414	C	19950911		
NO 8704757	A	19880516	NO 1987-4757	19871113
NO 172237	B	19930315		
NO 172237	C	19930623		
CN 87107875	A	19880525	CN 1987-107875	19871113
CN 1028991	B	19950621		
PRIORITY APPLN. INFO.:			CH 1986-4565	A 19861114
			EP 1987-116251	A 19871104

OTHER SOURCE(S): MARPAT 109:149535

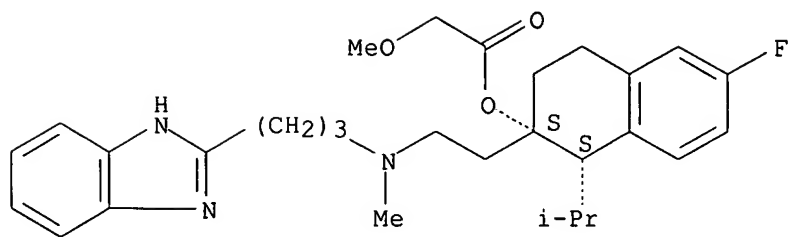
IT 116666-63-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiovascular agent)

RN 116666-63-8 HCAPLUS

CN Acetic acid, methoxy-, (1S,2S)-2-[2-[[3-(1H-benzimidazol-2-yl)propyl]methylamino]ethyl]-6-fluoro-1,2,3,4-tetrahydro-1-(1-methylethyl)-2-naphthalenyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl